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THIRD SERIES FOUNDED BY EDWARD JACKSON

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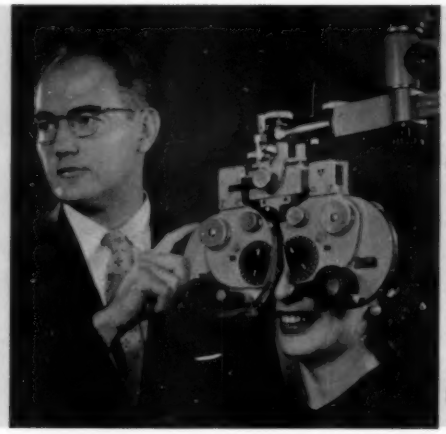

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References: (1) Morrison, W. H.: *Nebraska M. J.* **45**:106, 1960. (2) Perkins, E. S.: *Practitioner* **178**:575, 1957. (3) Tassman, W. S.: *U. S. Armed Forces M. J.* **10**:161, 1959. (4) Kamiya, S.: *Am. J. Ophth.* **42**:269, 1956. (5) Holland, R. W. B.: *Arch. Ophth.* **57**:214, 1957. (6) Benton, C. D., Jr.: *South M. J.* **51**:1562, 1958. (7) Blakiston's New Gould Medical Dictionary, ed. 2, New York, McGraw-Hill Book Company, Inc., 1956, p. 945. (8) Ostler, H. B., & Braley, A. E.: *J. Iowa M. Soc.* **44**:427, 1954.

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1. Cogan, J. E. H.: Proc. Roy. Soc. Med. *51*:927, 1958. 2. Jenkins, B. H.: South. M. J. *53*:44, 1960; discussion by Raiford, M. B. 3. Raiford, M. B.: J.M.A. Georgia *48*:163, 1959. 4. Rizzuti, A. B.: A.M.A. Arch. Ophth. *61*:135, 1959. 5. Thorpe, H. E.: Am. J. Ophth. *49*:531, 1960.

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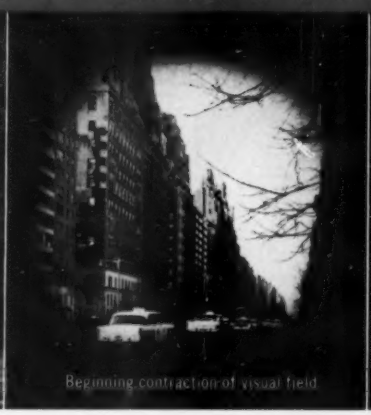
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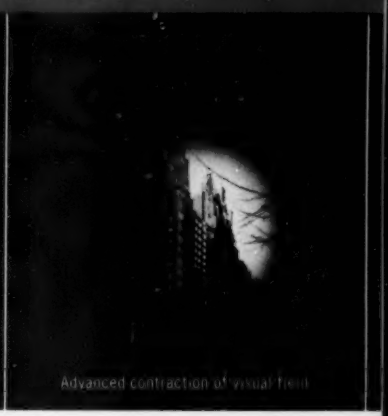
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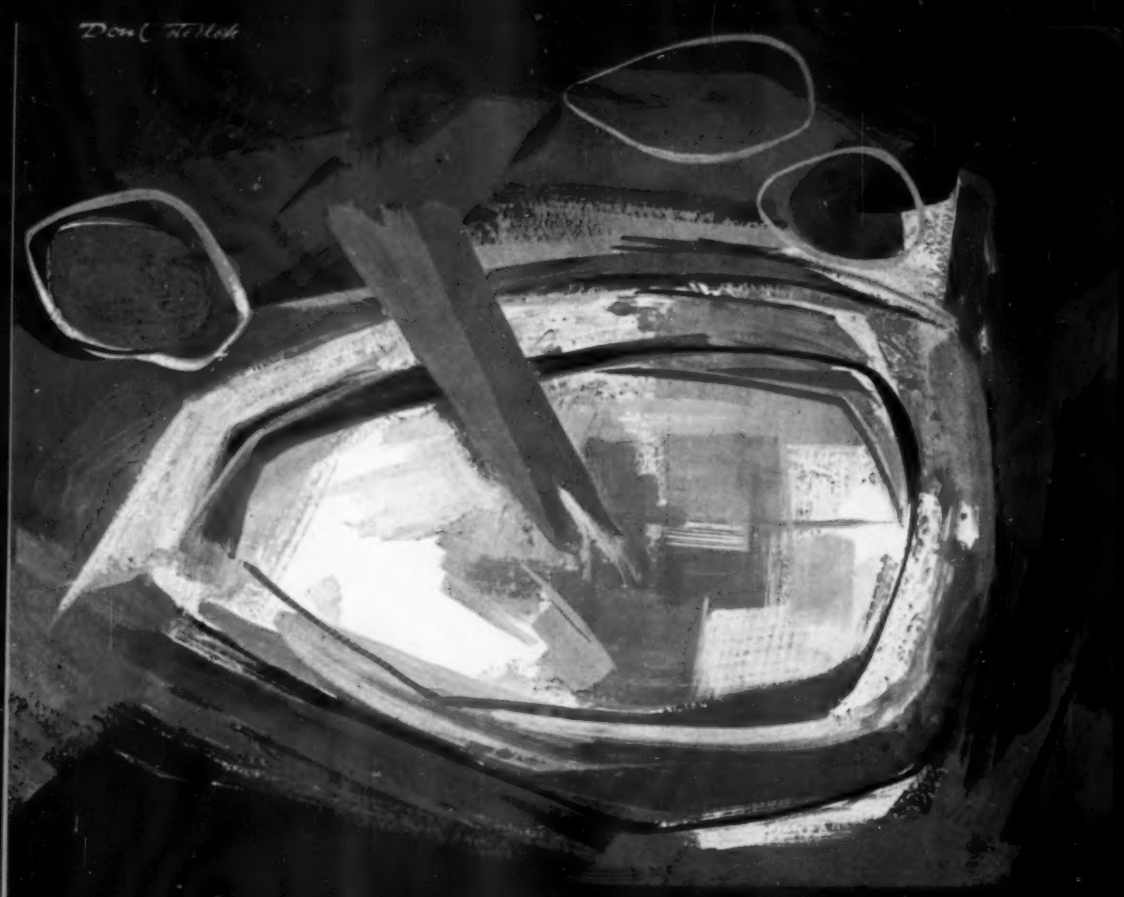

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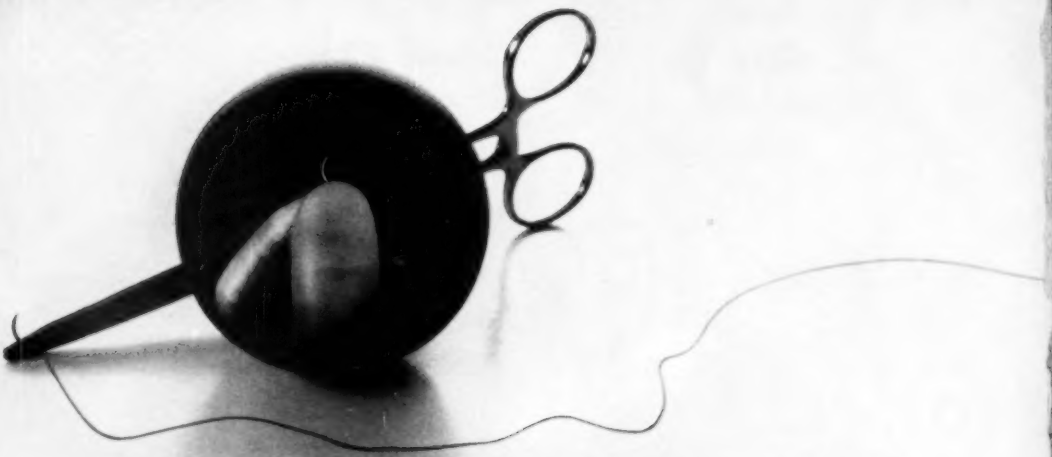

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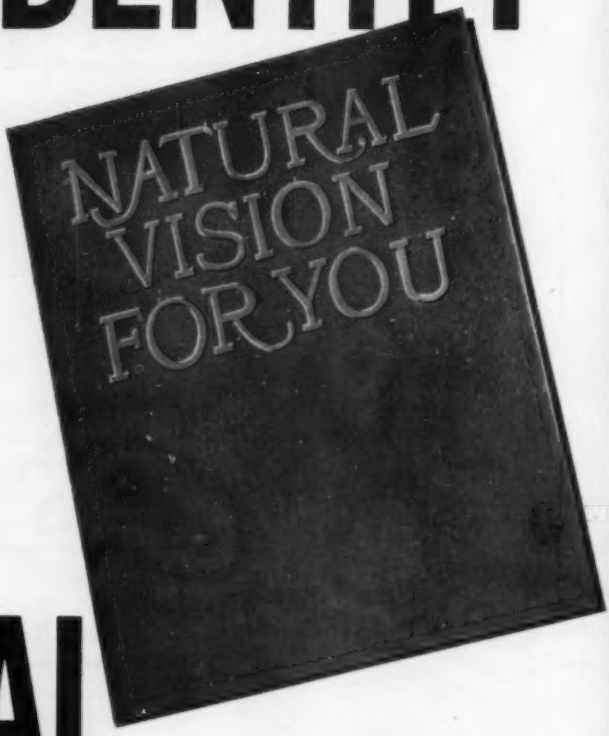

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AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 52 DECEMBER, 1961 NUMBER 6

SCLERAL SUPPORT OF THE POSTERIOR SCLERA*

PART II: CLINICAL RESULTS

BRIAN J. CURTIN, M.D.
New York

Part I of this study concerned itself with the effects of periscleral grafts of dense collagen tissues upon the animal eye.[1] These studies indicated that such grafts were well tolerated by the globe, produced no serious complications and did, in fact, effect support of the posterior sclera in excess of the physiologic limits of stress. These encouraging results were the basis of this pilot study of periscleral fascia grafts in clinical cases of progressive sclerectatic myopia.

CASE SELECTION

The first problem which presented itself in this study was that of the selection of cases. In considering both the nature of the disease process and the intended effect of the procedure, several criteria were immediately apparent. These were:

1. *The sclerectasia should be progressive.* Progression is loosely defined as an increase of one diopter per year of myopia.

2. *The myopia should be in a pathologic* range. In accordance with the presently accepted standards,[2] six diopters and above were so classified.

3. *There should be funduscopic evidence of posterior sclerectasia.* The ectasia should predominantly involve the macula or macula-disc area. This eliminated the inferior ectasias and nasal ectasias which are not infrequently seen.

4. *The prognosis without surgical intervention should be guarded.* This can be deduced by the history of constant increases in the myopia as well as the familial pattern of the disease.

5. *Evidence of chorioretinal degeneration should not be present.* Focal areas of choroidal atrophy or hemorrhage were thought to represent a relatively advanced stage of the disease and such cases were not selected for this study.

INSTRUMENTATION

On the basis of the preceding animal experiments, it was decided to retain the cruciate shape of the collagen graft. This was done for two reasons.

1. Although technically more difficult, such shape has the advantage of supporting a greater area of sclera at the posterior pole. This occurs by virtue of the graft capsule which extends from one graft arm to another in the region of the intersection. This capsule can be extremely dense.

2. The cruciate graft can be placed about the globe so that no muscle or tendon is interposed between it and sclera. This is of vital importance for graft snugness and, therefore, its reinforcing capabilities.

Several changes in instrumentation were necessary for the transition from experimental to clinical surgery because of essential differences in size, shape and other anatomic characteristics between the animal and human eye. New instruments have therefore evolved. These are: (1) curved retrobulbar forceps, with and without teeth, which were

* From the Myopia Clinic of the Manhattan Eye, Ear and Throat Hospital. This study was supported by a grant from the Eye Research Fund, and was presented in part at the VIII Congress of the Pan-Pacific Surgical Association, September 27-October 5, 1960, Honolulu, Hawaii.

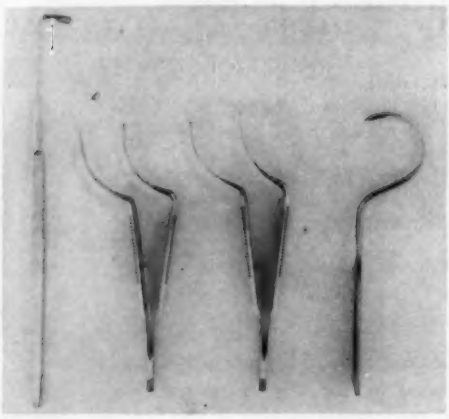

Fig. 1 (Curtin). Periscleral instruments. (Left to right) Muscle hook with eye; retrobulbar forceps, plain; retrobulbar forceps with teeth; fascia carrier.

devised for the handling of the graft at the posterior pole; (2) a hooked, eyed fascia carrier was developed for the passage of the graft arms about the nasal aspect of the globe; (3) an eyed muscle hook was found to be useful for the passage of the inferotemporal arm of the graft around the insertion of the inferior oblique (figs. 1 and 2).

Graft material

Fascia lata was used exclusively in this series of seven cases. It was chosen because of its availability in adequate amounts in both autologous and homologous tissues. It was distinctly preferable to sclera or tendon in its malleability and in the uniformity of its thickness and fiber bundle patterns. In one case, Case 7, reconstituted homologous fascia lata (U.S. Navy) was used. In the remaining six, autologous fascia was obtained in the usual manner, using a fascia stripper. The donor strip obtained measured 0.6 by 15 cm. The fascia was thoroughly cleaned of extraneous material and bisected from each end toward the center where a four-mm. area was left untouched. It was then placed in a moist chamber.

Operative technique

Following a lateral canthotomy, the specculum is inserted. A traction suture is placed at the nasal limbus.

A conjunctivo-tenon incision is made temporally from the lateral aspect of the superior rectus to the lateral aspect of the inferior rectus in an arc about seven mm. from the limbus. The lateral rectus is cleaned, sutured (4-0 chromic), severed from the globe and reflected laterally. The inferior oblique is hooked, carefully dissected and a traction suture passed around it.

A crescentric conjunctivo-tenon incision is made between the medial aspect of the superior rectus and the superior aspect of the medial rectus, about six mm. from the limbus. This same procedure is done in the inferonasal quadrant between the medial and inferior recti.

Traction sutures are passed around the three recti tendons. Meridional lamella scleral grooves are placed in each quadrant, equidistant from the recti insertions. These extend backward roughly six to seven mm.

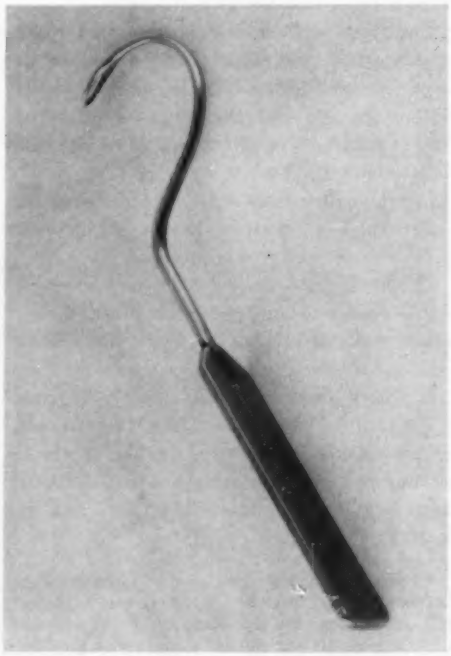

Fig. 2 (Curtin). The fascia carrier.

from the limbus. They measure three mm. equatorially and five to six mm. meridionally.

The fascia carrier is passed behind the globe from the superonasal quadrant out into the inferotemporal quadrant (nasal to superior oblique insertion; temporal to inferior oblique insertion.) The superonasal arm of the fascia graft is threaded through the "eye," and the carrier withdrawn back out into the superonasal quadrant. The fascia carrier is then passed behind the globe from the inferonasal quadrant out into the superotemporal quadrant (behind the inferior oblique), the inferonasal fascia arm is threaded through its "eye" and the carrier withdrawn.

The inferotemporal fascia arm is then passed nasally to the insertion of the inferior oblique by means of the special muscle hook and out into the inferotemporal quadrant. The superotemporal fascia arm is then passed forward into the superotemporal quadrant.

The four fascia arms are then put under gentle tension, especially the nasal and, if necessary, the midpoint of the graft is passed further nasally with retrobulbar forceps while the nasal arms are tensed. The fascia arms are trimmed to fit the prepared scleral grooves and sutured with 5-0 white silk. A locking stitch is necessary. The lateral rectus is resutured to the globe, the various traction sutures are removed and the conjunctival incisions closed with plain catgut (4-0) as is the canthotomy (figs. 3 to 12).

A corticosteroid ointment is instilled and a pressure patch applied. A binocular dressing is used.

Case reports

Case 1

L. B., a white girl, aged nine years.

Examination showed normal anterior segments and tension. Motility: Esotropia, O.D., 25Δ; Fundi: O.D., posterior sclerectasia with temporal scleral crescent; O.S., normal details. Refraction: (9/57) O.D., −13D. sph., 20/200; O.S., +0.5D. sph., 20/20. *Operation* (12/57). Periscleral graft, autologous fascia, O.D., resection lateral rectus, O.D. During the postoperative course, there was moderate chemosis and lid edema, lasting for five days. She was discharged on the fourth postoperative day. Refraction (5/60): O.D., −12D. sph., 20/70; O.S., −0.25D. sph., 20/20. Motility: Esotropia, O.D., 10Δ.

Case 2

A. O., a Puerto Rican girl, aged 15 years.

Examination showed normal anterior segments, tension and motility. Fundi: O.U., posterior sclerectasia with temporal choroidal crescents. Refraction (11/57): O.D., −11D. sph. ⌒ −3.5D. cyl. ax. 180°, 20/200; O.S., −9.5D. sph. ⌒ −4.5D. cyl. ax. 180°, 20/200.

Operation (4/58) Periscleral graft, autologous fascia, O.D. During the postoperative course, there was moderate chemosis, lid edema and proptosis lasting three days. She was discharged on the 11th postoperative day. Refraction (4/60): O.D., −11D. sph. ⌒ −3.5D. cyl. ax. 15°, 20/70; O.S., −9.5D. sph. ⌒ −3.5D. cyl. ax. 165°, 20/70.

Case 3

P. S., a Peurto Rican boy, aged eight years.

Examination showed normal anterior segments, tension and motility. Fundi: O.U., posterior sclerectasia with peripapillary conus. Refraction (7/58): O.D., −10D. sph. ⌒ −2.0D. cyl. ax. 15°, 20/70; O.S., −11D. sph. ⌒ −2.0D. cyl. ax. 165°, counting fingers.

Operation (8/58) Periscleral graft, autologous fascia, O.S. During the postoperative course, there was marked chemosis and lid edema which lasted six days. He was discharged on the seventh postoperative day. Refraction (9/60): O.D., −12.75D. sph. ⌒ −2.0D. cyl. ax. 180°, 20/80; O.S., −11D. sph. ⌒ −2.0D. cyl. ax. 180°, 20/100.

Case 4

P. L., a white boy, aged 12 years.

Examination showed normal anterior segments, tension and motility. Fundi: O.U., posterior sclerectasia with peripapillary conus. Refraction (8/58): O.D., −11.75D. sph. ⌒ −1.75D. cyl. ax. 170°, 20/200; O.S., −2.5D. sph., 20/30.

Operation (9/58). Periscleral graft, autologous fascia, O.D. The postoperative course was complicated by moderate chemosis and lid edema, which lasted four days. He was discharged on the sixth postoperative day. Refraction (1/60): O.D., −10D. sph. ⌒ −1.5D. cyl. ax. 175°, 20/100; O.S., −3.5D. sph., 20/25.

Case 5

G. H., a Negro boy, aged eight years.

Examination showed normal anterior segments, tension and motility. Fundi: O.U., posterior sclerectasia with peripapillary conus. Refraction (7/58): O.D., −12D. sph. ⌒ −2.5D. cyl. ax. 180°, 20/60; O.S., −6.0D. sph. ⌒ −2.0D. cyl. ax. 180°, 20/30.

Operation (11/58) Periscleral graft, autologous fascia, O.D. The postoperative course was complicated by a hematoma of the right thigh. On the sixth day postoperative, the hematoma was evacuated and a drain inserted. He was discharged on the 11th postoperative day. Refraction (3/60):

O.D., −10.5D. sph. ⊂ −2.5D. cyl. ax. 25°, 20/50; O.S., −6.0D. sph. ⊂ −2.5D. cyl. ax. 155°, 20/30.

CASE 6

D. H., a Negro girl, aged four years.

Examination showed normal anterior segments and tension. Motility: alternating esotropia, 20-25Δ. Fundi: O.U., posterior sclerectasia with temporal scleral and choroidal crescents. Refraction (5/59): O.D., −14.75D. illiterate (spherical equivalent); O.S., −14.75D. illiterate (spherical equivalent).

Operation (7/59). Periscleral graft, autologous fascia, O.D. Recession, medial rectus and resection, lateral rectus, O.D. The postoperative course was complicated by moderate chemosis and lid edema, lasting six days. She was discharged on the seventh postoperative day. Refraction (8/60): O.D.,

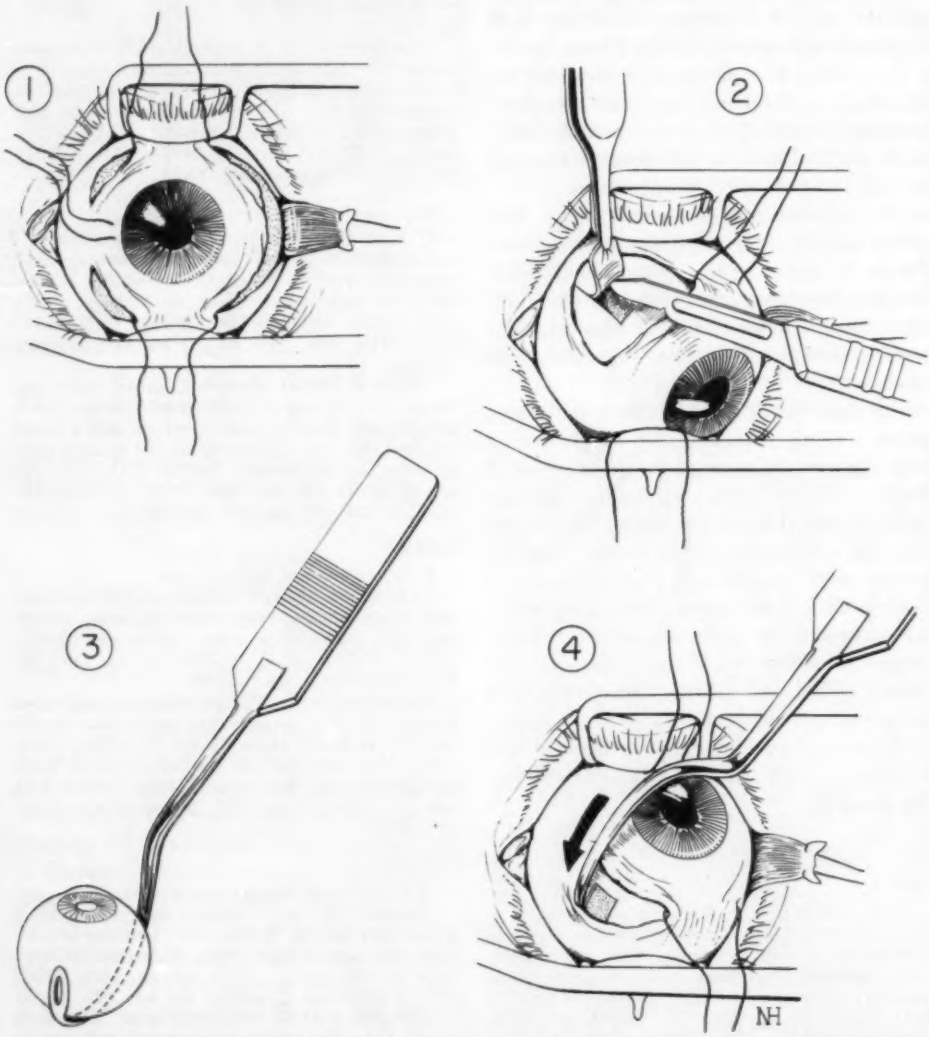

Plate 1 (Curtin). (1) Preparation of the globe for graft. Conjunctiva-tenon incisions over lateral aspect, superior and inferior nasal quadrants. (2) Lamellar sclerectomy in inferonasal quadrant. (3) Diagram of fascia carrier in position about globe. (4) Insertion of fascia carrier into superonasal quadrant.

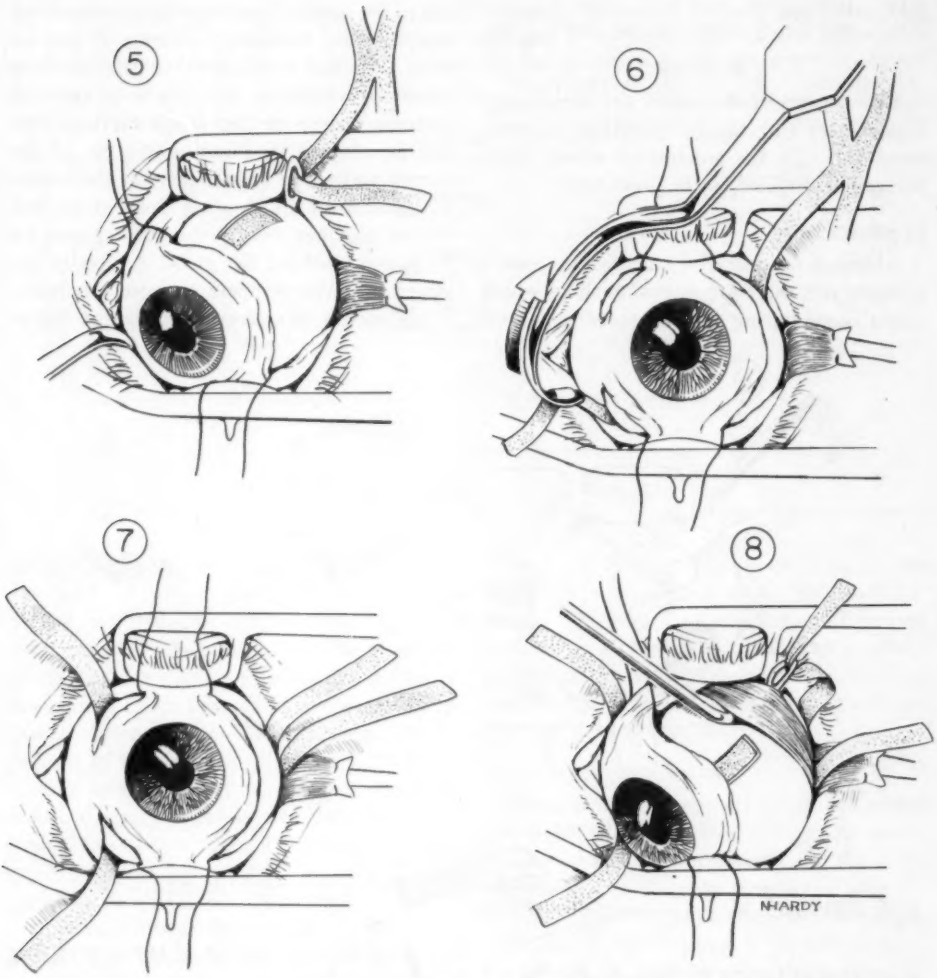

Plate 2 (Curtin). (5) The superonasal arm of graft is threaded through the eye of the fascia carrier. (6) Carrier, with graft arm, brought out into the superonasal quadrant. (7) Superior and inferior nasal graft arms in position. (8) Passage of inferotemporal arm around the insertion of the inferior oblique by means of the muscle hook with eye.

−13.25D. sph. ⊃ −1.0D. cyl. ax. 180°, illiterate; O.S., −16.25D. sph. ⊃ −3.0D. cyl. ax. 60°, illiterate Motility: Esophoria 10Δ

CASE 7

G. R., a Negro boy, aged three years.

Examination showed normal anterior segments, with some bluish tint in sclera. Tension and motility were normal. Fundi: O.U., posterior sclerectasia with peripapillary conus. General: bilateral pes planus, moderate extensibility of skin and ligaments. Refraction (10/59): O.D., −19.5D., illiterate (spherical equivalent); O.S., −17.5D., illiterate (spherical equivalent).

Operation (12/59). Periscleral graft, homologous fascia, O.D. The postoperative course was complicated by moderate chemosis and lid edema, lasting five days. He was discharged on the sixth postoperative day. A late complication developed when a conjunctival granuloma appeared some three weeks postoperatively and resolved spontaneously after three weeks. Refraction (8/60):

O.D., −16D. sph. ⊂ −2.0D. cyl. ax. 180°, illiterate;
O.S., −18D. sph. ⊂ −2.0D. cyl. ax. 180° illiterate.

Results

Two aspects of this study are of primary importance: (1) the complications encountered and (2) the amount of scleral reinforcement obtained by the procedure.

Complications

Although no operative complications were encountered, there are several mishaps which might occur during such a procedure. Damage to the orbital blood vessels with resultant bleeding and choroidal ischemia is one of these. This has not occurred to date. Another serious complication is rupture of the thin posterior sclera by the fascia carrier. This can be avoided by blunting the tip of the carrier and, more importantly, by the operative maneuver of rotating both globe and carrier together during the greater part of its passage behind the globe. A greatly enlarged posterior segment may well contraindicate such a maneuver. The highest degree

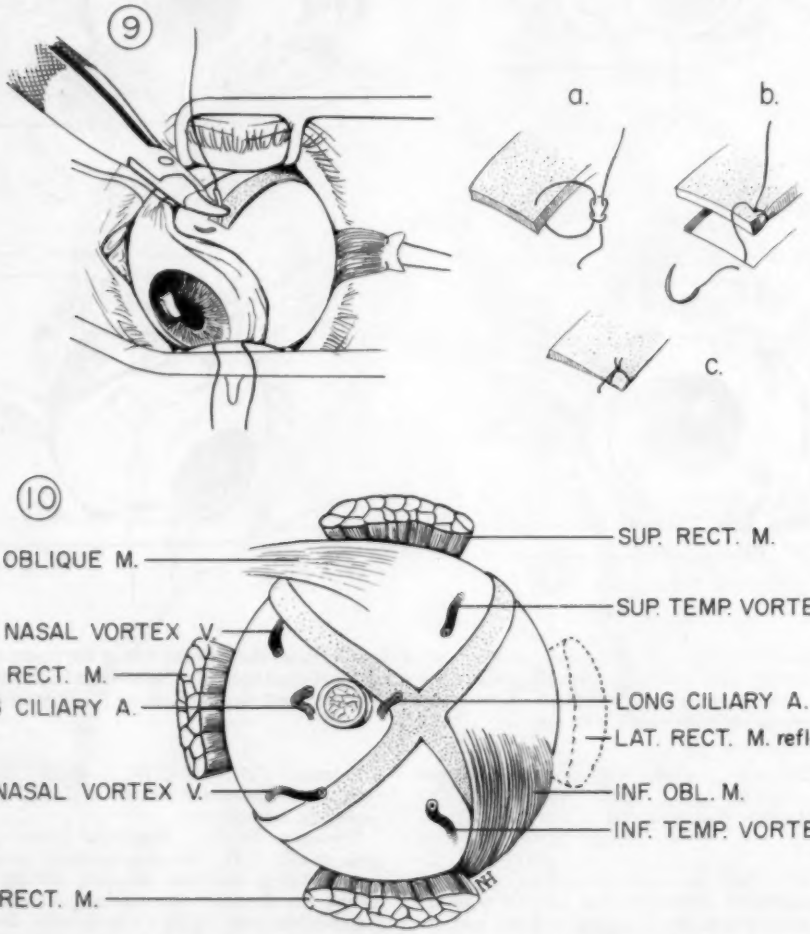

Plate 3 (Curtin). (9) Locking suture technique for the insertion of graft arm into sclerectomy bed. (10) Graft in place about globe as seen from posterior aspect.

TABLE 1

SURVEY OF CASES

Case	Age (yr.)	Sex	Operation	Follow-up (Mo.)	Control eye diopter change	Operated eye diopter change
1	9	F	Autologous fascia graft	33	−0.25	+1.00
2	15	F	Autologous fascia graft	29	0.00	0.00
3	8	M	Autologous fascia graft	25	−2.75	0.00
4	12	M	Autologous fascia graft	24	−1.00	+1.75
5	8	M	Autologous fascia graft	22	0.00	+1.25
6	4	F	Autologous fascia graft	14	−2.50	+1.00
7	5	M	Homologous fascia lata	11	−1.50	+2.50

of myopia operated to date with this method has been −19.00 diopters.

The postoperative complications have not been serious. The most frequently observed reactions were chemosis, lid edema and some discomfort on motion of the eye in the early postoperative course. This occurred in 86 percent of the cases in this series. These reactions were ascribed to a tenonitis which subsided after several days of treatment. The topical use of corticosteroids and warm compresses, as well as systemic salicylates, was found to be effective in its control.

One case displayed a mild proptosis together with the signs just mentioned. This abated in about three days and was attributed to tissue reaction in the retrobulbar area. While retrobulbar hemorrhage was considered here, the absence of bleeding during surgery, together with the mild extent of the proptosis and its rapid recession made this diagnosis seem improbable.

One other case developed a conjunctival granuloma in the late postoperative period. This was probably the result of a dehiscence in the conjunctival wound. It disappeared spontaneously after three weeks.

Although not an ocular complication, one other case developed a hematoma of the thigh where the donor fascia had been obtained. This, by far, was the most vexing problem encountered, necessitating a second general anesthesia for the evacuation of blood and the insertion of a drain. Prompt and uneventful healing then ensued.

SCLERAL REINFORCEMENT

Because of the complexity of equipment and technique in the use of objective methods of measuring anteroposterior diameter, refraction was the only means available for this, which introduced a considerable margin of error in the evaluation of scleral reinforcement. In spite of this, the results obtained are of singular interest.

The follow-ups on the reported cases ranged from 11 to 33 months, with an average of 22.5 months. During this time, the unoperated control eyes increased in myopia in a range from 0.0D. to −2.75D. with an average of −1.14D. The operated eyes, however, showed a reduction in myopia in a range of from 0.0D. to +2.5D. with an average of +1.07D.

DISCUSSION

There are three areas of weakness in this

TABLE 2

COMPLICATIONS

		Percent
Ocular:	Tenonitis	86
	Proptosis	14
	Conjunctival granuloma	14
Other:	Hematoma, thigh	17

study. The relatively small series of cases and the limited follow-up periods make definitive deductions somewhat hazardous. Still another area of uncertainty is that of relying upon refraction data alone to assess the effectiveness of the surgery. The variables of refraction in the highly myopic child who is often amblyopic are well known to all practicing ophthalmologists.

In spite of these limitations, the study does impart a certain amount of guarded optimism for the future of this work. The absence of serious complications reported herein should result in a broader and more determined attack on the problem of postectasia. The minor complications incurred in this series support the results of previous animal studies.

Of the serious complications reported in clinical work to date, the one case of globe perforation reported[3] occurred in an eye that measured 24 diopters of myopia. This would underscore the necessity of operating earlier in the progress of the disease. An extremely thin, soft sclera in a greatly elongated eye would make the procedure much more dangerous and difficult. At such a degree of postectasia, it is also quite likely that the prerequisite conditions for chorioretinal degeneration are already present.

In judging the effectiveness of the graft, we are presently forced to rely on refractive data which have a considerable margin of error. A simple, accurate, objective technique of measuring the anteroposterior diameter is needed. None is presently available but, with some modifications, sonography may eventually prove of great value in such application. We can cite, however, the progression of myopia in the control eye compared to the absence of progression in the operated one. These results further are augmented by those of Malbran[3] and Borley and Snyder[4] in which no progression ensued after surgery.

There are two conceivable methods whereby the graft effects reinforcement:

A mechanical effect would appear to be indisputable. Animal experiments have demonstrated the ability of the graft to withstand traction well in excess of physiologic limits. Both Malbran and Borley have had occasion to examine periscleral grafts months after their insertion and in both instances they were found to have incorporated themselves well and showed little tendency to absorption.

Another method whereby scleral support can be effected might be termed biochemical. The presence of normal graft collagen tissue in contiguity with abnormal host collagen[5,6] might effect a diffusion of needed metabolites, notably sulfated mucopolysaccharides and certain amino-acid linkages, which the recipient tissue may be unable either to synthesize or incorporate into its structure. This would be somewhat analogous to the tissue therapy of Filatov.

By far the most interesting result obtained by the periscleral graft was not anticipated. This was the apparent reversal of the sclerectatic process, with a resulting reduction in myopia. This occurred in 70 percent of the cases operated. In Malbran's series it occurred in 77 per cent of a series of 14 operations. The most likely explanation of this reduction in myopia lies in the postoperative shrinkage of the graft and its capsule. The animal experiments of Part I[1] indicated that

TABLE 3

SCLERAL REINFORCEMENT

	Range	Average
Postoperative follow-up	11 to 33 mo.	22.5 mo.
Refraction changes		
Control Eyes	0.00 to −2.75 diopters	−1.14 diopters
Operated Eyes	0.00 to +2.50 diopters	+1.07 diopters

such graft contraction occurred routinely unless muscle was interposed between graft and sclera. Such shrinkage of grafted connective tissue is known in other fields of surgery.[7,8] The shrinkage of a periscleral collagen graft would, in effect, produce a reverse shear force on the strained sclera. Another possible cause of this reduction in refraction is a change in corneal curvature secondary to the insertion of the graft arms into the anterior sclera.

There is, of course, also the possibility of errors in the performance of these difficult refractions producing an apparent reduction in myopia. This would not, however, appear to be likely. Larger series using more exact, preferably objective, measurements of the anteroposterior diameter of the globe will have to be completed to resolve these questions.

The problem of the ideal donor graft material remains unanswered at this time. Tendon, fascia lata and sclera have all been effectively used in man at this time but the efficacy of one over the other still hinges more on the particular desires and technique of the operator than upon any scientific basis. In this regard, Malbran's results bear special mention. Using autologous tendon in a single, vertical belt or sling, he obtained reductions in myopia of up to eight diopters. This is considerably greater than the maximum of 2.5D. obtained in this series wherein a cruciate graft of homologous fascia lata was used (Case 7). The late results obtained by the Barraquers[9] using a horizontal strip of sclera may prove illuminating in this regard. They place a six-mm. trephine opening in a partly bisected strip of sclera 12-mm. wide to accommodate the optic nerve. A very large area of sclera is thereby reinforced.

The arguments for autologous collagen tissues in preference to homologous are few. Autologous grafts are thought to take better with less reaction and are therefore said to be preferable if a choice is present. The animal experiments seemed to corroborate this. However, in the actual clinical case, homologous tissues may well be preferable. They are available without additional trauma to the patient. Too, with their use, a more mature and hence less extensible tissue can be used for reinforcement. Lastly, they avoid the possibility of using abnormal donor tissue if systemic collagen dysplasia is present. Case 7 of this series is an example of this situation. Only extensive clinical trials will determine the ideal graft material. Certainly, shrinkage is a factor which may well be decisive and yet the one about which we now know the least.

The ability to predict accurately further sclerectasia would be of decided benefit in case selection. The family and personal history are the only indicators now available. A study was undertaken by Bussey and Curtin several years ago at the Myopia Clinic of the Manhattan Eye, Ear and Throat Hospital in which a correlation was attempted between the progress of myopia and ocular rigidity. This study was abandoned after two years because of the inaccuracies of the Schiøtz tonometer readings in the children tested. No deductions could be drawn from the data obtained.

Another area in which additional work is needed is that of correlating fundus changes with the location of the posterior staphyloma. While it may always be desirable to reinforce the sclera in the macular region, it may be of equal importance to support the area of greatest ectasia wherever it may be: nasal, temporal or inferior to the optic nerve. The surgery may need to be altered to suit individual cases for maximum effect.

It will take many years of research by many investigators to answer these, the more superficial problems, in this field. In the mean time, the cruciate periscleral fascia graft can be considered a relatively safe and scientifically rational method of treatment for a disease of high incidence and grave prognosis for which no effective therapy now exists.

Summary

The results are reported of an initial series of seven cases in which a periscleral cruciate graft of fascia lata was used to con-

trol sclerectatic myopia. The criteria for case selection and the operative technique are outlined in detail. In spite of the small number of cases, the somewhat limited follow-up period and the absence of an objective method of measuring scleral reinforcement, it is apparent that the procedure is innocuous and does produce scleral reinforcement. These results are examined in respect to the previously reported work in this field. The areas in need of further study are also discussed. These include the choice of graft material, improved methods of estimating anteroposterior diameter of the globe, and better criteria for case selection.

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VALUE OF RETINAL ARTERY PRESSURE DETERMINATION*

In the diagnosis of internal carotid artery thrombosis

The role of the carotid compression test

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The disclosure that internal carotid artery thrombosis is not infrequently the cause of a brain stroke has changed the general opinion concerning the pathogenesis of cerebral infarction. Thus, it has been revealed, that a brain stroke can be a consequence of an extracranial arterial occlusion; also in such cases the cerebral infarction may not be entirely due to an embolus or thrombus, but also to hemodynamic crises, for instance to a general blood pressure drop.

The accumulating data concerning the so-called recurrent or episodic form of carotid thrombosis, with quite long, sometimes almost symptomless, periods interrupted by transient "attacks" of hemiparesis or monocular blindness, drew more attention to the pre-ictal phase of cerebrovascular disease. Since the "transient ischemic attacks," previously supposed to be caused by vasospasm or embolism, should rather be dealt with as prodromes of a stroke, the exact diagnosis of their causes would permit prophylactic treatment, medical and/or surgical, to prevent an irreversible damage to cerebral tissue. Many efforts have, therefore, been made to acquire as early as possible the precise diagnosis of the nature and localization of

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the vascular lesion, as well as the—in each case—different condition of the collateral circulation. Even cerebral angiography, which is the most important aid to diagnosis, still does not always resolve the diagnostic doubts. Besides, in cases of arterial occlusion, such a procedure is not without danger to the patient.

For these reasons, much interest has been shown in recent years in retinal artery pressure determination, which has proved to be a safe and valuable diagnostic method in cases of cerebrovascular insufficiency. It is today rather generally accepted that, if the clinical picture indicates internal carotid artery thrombosis, revealment of at least a 15-percent lower pressure in the homolateral retinal artery confirms the diagnosis,[1-23] thus sometimes avoiding cerebral angiography, especially when no operation is planned.[24-26]

Still, the problem is not so simple as it seems because, not infrequently, one has to deal with cases in which the retinal artery pressure is equal in both eyes, in spite of the clinical data, strongly indicating occlusion of the internal carotid artery which may even be verified by angiography. The number of such cases is remarkable, 20 to 30 percent according to the rather considerable series of Hollenhorst[12-14] and other authors.[22, 23, 27] This fact is, apparently at least, seriously restricting the value of ophthalmodynamometry as a method for the diagnosis of carotid thrombosis. It seems, therefore, worthwhile to consider this problem more thoroughly.

To appraise the mechanism of retinal artery pressure levels becoming equal in both eyes, it is necessary to consider the role that the collateral circulation plays in cases of internal carotid occlusion. One should remember that, when the internal carotid arteries are patent, the retinal artery pressure, as a rule, reflects the pressure level in the homolateral internal carotid artery; this must not always be so when this artery is occluded. Then it depends mostly on the efficiency of the collateral circulation which is derived mainly from the opposite internal carotid artery, further from the homolateral external carotid and from the basilar system. Thus it must be concluded that, in cases of carotid artery occlusion, the pressure level in the homolateral retinal artery is the resultant of the pressure in the occluded internal carotid artery, as well as of the pressure of the blood stream flowing from the sources of the collateral circulation. It is then evident that, if the general blood pressure level is sufficiently high and there is no obstruction on the way from the sources of the collateral circulation to the occluded internal carotid artery, the retinal artery pressure in both eyes might become equal. The majority of authors think it sufficient to explain this fact,[12-14, 16, 22, 23, 27, 28] without considering the possibility of applying ophthalmodynamometry to achieve a correct diagnosis in cases in which the retinal artery pressure is equal.

In such cases, we have applied the carotid compression test in order to cause a transient breakdown of the collateral circulation. It appeared that, when individuals with patent internal carotid arteries were submitted to digital compression of one of the arteries, the retinal artery pressure *dropped* on the homolateral and *rose* on the opposite side,[26, 29] yet when a patent artery of a patient with carotid thrombosis was compressed, the retinal artery pressure dropped in both eyes.[25, 26]

Case reports

Case 1

M. H., a 64-year-old man had a three-year history of transient ischemic attacks, followed by a cerebral stroke in 1957. During his first stay in the hospital, thrombosis of the left internal carotid artery was revealed by angiography.

The ophthalmodynamometric examination carried out one year later showed the retinal artery pressure in the left eye to be about 35-percent lower than in the right one. The control examination carried out nine months later showed equal retinal artery pressure levels: R.E., 80/52 mm. Hg; L.E., 78/58 mm. Hg. General blood pressure, 140/80 mm. Hg. Then, the right carotid artery, that is, the patent one, was compressed with the finger. The ophthalmodynamometric examination, carried out during the compression, lasting one minute, showed: R.E., 55/26 mm. Hg; L.E., 52/28 mm. Hg. The general blood pressure level remained un-

changed. Thus, compression of a patent carotid artery caused a retinal artery pressure drop in both eyes. The compression of the occluded artery caused no change in the retinal artery pressure level.

CASE 2

S. W., a 43-year-old man, in 1956, suffered a brain stroke with left hemiparesis. Cerebral angiography two years later showed an occlusion of the right internal carotid artery. This examination did not, however, show quite reliably whether it was a thrombosis, a spasm or a hematoma following puncture of the artery.

The ophthalmodynamometric examination showed equal retinal artery pressure levels in both eyes, 96/68 mm. Hg, and a general blood pressure of 140/100 mm. Hg. It was then decided to perform the carotid compression test.

Compression of the left carotid artery (one minute), retinal artery pressure: R.E., 46/21 mm. Hg; L.E., 41/19 mm. Hg. During the test, the blood pressure dropped to 120/70 mm. Hg, which means that the general diastolic pressure dropped 30-percent. However, the diastolic pressure in both retinal arteries showed a drop of 65-percent, which means about 35-percent of the real drop.

In this case also, a pressure drop in both retinal arteries was achieved by compression of the patent artery, which confirmed the diagnosis of a right internal carotid artery thrombosis. A compression of the occluded artery was followed by a small drop in the retinal artery pressure level on this side.

In cases in which internal carotid artery thrombosis is suspected and the neurologic symptoms and signs indicate the side of occlusion but the compression on the opposite carotid does not confirm this diagnosis, compression of the common carotid artery on the side of suspected occlusion will often be confirmatory. By this means, it is sometimes possible to demonstrate that the collateral circulation derives mainly from the external carotid artery, homolateral to the occluded internal carotid. This fact is well known from the angiographic findings and quite understandable in light of phylogenetic studies and experimental work.[20, 21]

CASE 3

J. S., a 65-year-old man, suffered a brain stroke with right hemiparesis, preceded by "transient ischemic attacks." The ophthalmodynamometric test, which was carried out some months later showed: R.E., 80/45 mm. Hg; L.E., 84/42 mm. Hg. Compression of the right carotid artery, which according to the clinical estimation was patent, showed a large drop on the compressed side and a very small drop on the opposite side. Compression of the left carotid artery, most probably a homolateral one with an occluded internal carotid artery, caused the left optic disc immediately to turn pale. The examination was stopped because the patient felt badly.

In spite of the lack of precise data in this case, it seems apparent that the main source of the collateral circulation was the external carotid artery on the side of the thrombosis.

These cases seem to indicate that ophthalmodynamometry can play an important role in the 20 to 30 percent of cases of internal carotid artery thrombosis in which (based on reports in the literature) it was thought to be of no diagnostic value. The only thorough record recommending the use of the carotid compression test during the ophthalmodynamometric examination in cases of carotid thrombosis is the publication of Miletti[3] which was referred to, in this respect, by surprisingly few authors.[5, 15]

Used as a control group were selected cases of intracranial aneurysms, in which an equal retinal artery pressure level was found in both eyes at various periods after ligation of the carotid artery. The examinations carried out in this group confirmed the importance of using the carotid compression test during ophthalmodynamometry for the diagnosis of carotid occlusion. In such cases, in which in a very short period after the ligation of the carotid artery the retinal artery pressure becomes equalized in both eyes, it is possible to show (using the carotid compression test during the ophthalmodynamometric examination) whether this is the result of a fairly efficient collateral circulation or the slipping down of the vascular ligature.[32]

Two essential details, connected mainly with the carotid compression test, must be borne in mind: (1) Although this test proved to be safe in a considerable number of patients, as is reported by Webster and others,[33, 34] nevertheless, it must be carried out very carefully, as it causes, in case of a

complete occlusion of the internal carotid artery, a temporary closure of one more source of the cerebrovascular circulation. (2) It should be emphasized that manipulations in the region of the carotid sinus may cause serious changes in the general blood pressure, which, of course, influence the retinal artery pressure level. Not to consider these factors in interpreting the measurements might result in diagnostic errors; therefore, it is also necessary to record the general blood pressure[26,29] during the determination of the retinal artery pressure.

Conclusions

1. Determination of the retinal artery pressure is valuable in the diagnosis of internal carotid artery thrombosis not only when pressure differences exist but also when the retinal artery pressure level is equal in both eyes. In such cases the diagnosis can be confirmed by using the carotid compression test during the ophthalmodynamometric examination.

2. Taking the retinal artery pressure determination using the carotid compression test simultaneously can reveal whether the main source of collateral circulation is the opposite internal carotid artery or the external carotid artery homolateral to the occluded internal carotid artery.

3. A proper diagnosis—particularly when using the carotid compression test—can be achieved only if each retinal artery pressure determination can be referred to a simultaneous measurement of the general blood pressure in the radial arteries.

Summary

The role of the retinal artery pressure determination in the diagnosis of internal carotid artery thrombosis is discussed and particular emphasis is given to those cases in which the retinal artery pressure level is equal in both eyes.

We are of the opinion that, in cases of carotid occlusion, the homolateral retinal artery pressure is the consequence of the pressure in the occluded internal carotid artery and of the blood pressure stream coming from the sources of collateral circulation. It means that the retinal artery pressure in these cases can or cannot reflect the pressure in the occluded carotid artery. Thus, it is evident that the difference between the retinal artery pressure level in both eyes can be smaller than the 15 percent accepted in the literature or that there may be no difference at all. In such cases a proper diagnosis can be achieved by means of ophthalmodynamometric examination but simultaneous use of the carotid compression test is necessary. During digital compression of the presumably patent carotid artery, the pressure drops not only in the retinal artery on the side of the compression but in the retinal arteries in both eyes (Cases 1 and 2). In Case 3, it is shown that the main source of collateral circulation is the external carotid artery homolateral to the occluded internal carotid artery.

A correct diagnosis, particularly when the carotid compression test is applied, can be achieved only if each retinal artery pressure determination is referred to the simultaneous general blood pressure level.

*Narutowicza 95.**

All examinations were carried out using the Sobański ophthalmodynamometer.

* Dr. Szapiro's address.

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THE MANAGEMENT OF GLAUCOMA IN THE INDIGENT CLINIC PATIENT*

WITH ECHOTHIOPHATE IODIDE

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This report presents the results obtained in the use of echothiophate (Phospholine) iodide in a series of 43 eyes of 24 patients suffering from glaucoma. With two exceptions, these were patients whose intraocular pressure had remained uncontrolled under a regime which usually included pilocarpine (four percent) eserine (one percent) and acetazolamide (250 mg. q.i.d.). The observations are representative of those to be expected with the indigent clinic patient and require some comment in order better to appreciate the results obtained.

These patients are uneducated, on some form of public assistance and with little understanding of their disease even to the point of not remembering the word, glaucoma. Field is a vague, esoteric entity, the meaning of which they sometimes ultimately grasp as central vision becomes impaired. Many of these patients should have had surgery but this was refused even after repeated entreaties. In spite of directions from the medical staff, they appear irregularly every one to three months for an afternoon of tension taking and talk with friends and are totally unconcerned about an increase in the blindspot or an enlarging scotoma. Usually, they have not used their drops regularly, in which case their tensions are out of control and their pupils not miotic; as a result, they will have to submit to an embarrassing scolding by one of the residents. Eventually, however, they remember to take their medication the night before and the morning of their clinic visit so that their tensions are fair, their pupils miotic, the doctors agreeable, the patient pleased and their fields further constricted.

Recent reports on echothiophate iodide, stressing its long duration of action and ability to control glaucoma where conventional drugs have failed,[1-7] suggested the desirability of a trial of this drug in these difficult-to-manage cases. It was felt that a drug which was taken twice a day at the most might be used frequently enough by the patients to control their tensions. Also, since no drop instillation would be required during the late morning or early afternoon, the medication could be left at home. Short-acting drops, in contrast, would have to be carried about during the daily activities and would be subject to loss or breakage. Such obvious practical considerations cannot safely be ignored in patients of this kind.

Narrow-angle glaucoma has proven to be uncommon in our Negro clinic patients and in this series there were no cases. In the past, we had felt that the long-acting cholinesterase inhibitors were primarily indicated in open-angle glaucoma patients if they were aphakic or had had a glaucoma operation; however, as the results will show, these drugs proved particularly useful in clinic patients with uncomplicated open-angle glaucoma because of their casual attitude toward multiple drop instillations, progressive field loss and their refusal of further operative procedures.

RESULTS

Observations and results are given in Table 1 which is subdivided as follows:

Patient-age-race-sex. The average age was 65 years, range 46 to 79 years, except for one case of an epithelial downgrowth occurring

* From the Eye Clinic, Philadelphia General Hospital. The Phospholine Iodide was supplied by Campbell Pharmaceuticals, Inc., New York.

TABLE 1

SUMMARY OF OBSERVATIONS AND RESULTS*

Patient Age-Race-Sex	Type of Glaucoma	Previous Medication	Previous Surgical Procedures	Vision & Fields	Previous Tension (mm. Hg.)	Dose & Frequency of Echothiophate Iodide	Tensions on Echothiophate Iodide	Efficacy of Echothiophate Iodide†	Side-Effects	Remarks
A.B. 66-C-F	O.A.	OU-P 4%, Es 1% qid Aceta 250 mg qid	None	OD LP OS 10°	OU 40	OU—0.25% bid	OU 42	0	None	Grade I diabetic fundi. Also on acetazolamid 250 mg. qid.
P.B. 65-W-F	O.A.	OU-P 3%, Es 1% qid	None	OD 6/6 OS 6/9 Full fields	OD 22 OS 26	OU—0.25% qd	OD 20 OS 24	+	None	Grade II diabetic. Placed on echothiophate iodide because of missed drops
A.C. 73-C-M	O.A.	OU-P 3%, Es 1% qid Aceta 250 mg qid	OU Iridencleisis	OD 6/60 OS 6/60 OD 20° field OS Bjerrum scotoma	OD 26 OS 26	OD—0.25% qd OS —0.25% bid	OD 18 OS 20	+	None	Also on acetazolamide 125 mg qid
J.F. 60-C-M	O.A.	OU-P 4% qid Aceta 125 mg tid	OD Iridencleisis & cataract OS Elliot trephine & cataract	OD 1/60 OS shadows	OD 26 OS 30	OU—0.25% qd	OD 16 OS 19	+	None	OD Macular degeneration
A.F. 73-C-M	O.A.	OU-P 4%, Es 1% qid Aceta 250 mg qid		OD 6/60 OS 6/60 10° fields	OD 36 OS 36	OU—0.25% bid	OD 19 OS 19	+	None	Also on acetazolamide 250 mg qid
R.G. 70-C-F	O.A.	OU-P 3%, Es 1% qid Aceta 125 mg qid	OU Iridencleisis	OD 6/15 OS 6/9 OU Bjerrum scotoma	OD 26 OS 26	OU—0.25% bid	OU 26	0	None	OU Excellent initial response. Acetazolamide 125 mg qid
A.H. 72-C-F	O.A.	OU-P 4%, Es 1% qid Aceta 250 mg qid	OS Iridencleisis	OD Bjerrum scotoma OS Baring of blind spot	OD 33 OS 33	OU—0.25% bid	OD 28 OS 26	+	None	Refuses to take echothiophate iodide as it cuts her vision down too much (OU early lens changes).
W.J. 70-C-M	O.A.	OU-P 4%, Es 1% qid	OS Cataract extraction with basal iridectomy	Full fields	OD 26 OS 26	OS—0.25% qd	OD 22 OS 16	+	None	OD-P 4%, Es 1% continued
T.L. 63-W-F	O.A.	OU-P 3% qid	None	OU Bjerrum scotoma	OD 24 OS 30	OU—0.25% hs	OD 26 OS 26	0	Headaches	Echothiophate iodide was stopped because of protracted headaches
M.L. 61-C-F	O.A.	OU-P 4%, ES 1%	None	OD CF OS 6/9 OD 15° OS Arcuate scotoma	OD 22 OS 28	OS—0.25% bid	OS 33	−	Headaches	Grade 2 diabetic fundi
L.M. 60-W-M	O.A.	None	OD Scheie procedure OS Iridencleisis	OD 6/6 OS LP Full Field#	OD 33 OS 33	OU—0.25% qd	OD 26 OS 19	+	None	
C.O. 67-C-M	O.A.	None	OU Iridencleisis	OD 6/12 OS 6/15 Advanced glaucomatous changes	OD 36 OS 26	OU—0.25% hs	OD 19 OS 22	+	Headaches	Patient had severe headaches with 0.25%. Cut to 0.125% and later increased to 0.25% qd. No headaches at present

* Abbreviations: O.A.—chronic simple open angle; P—pilocarpine; Es—eserine; Aceta—aceta zolamide; DFP—isoflurophate; CF—counts fingers; LP—light perception; qd—once a day; hs—before retiring; diabetic fundi: grade i—minimal, grade ii—slightly more advanced, grade iii—moderate, grade iv—advanced.

† See text for explanation of symbols.

Patient Age-Race-Sex	Type of Glaucoma	Previous Medication	Previous Surgical Procedures	Vision & Fields	Previous Tension (mm. Hg.)	Dose & Frequency of Echothiophate Iodide	Tensions on Echothiophate Iodide	Efficacy of Echothiophate Iodide†	Side-Effects	Remarks
H.P. 77-C-F	O.A.	O-P 3%, Es 1% qid	None	OD 6/9 OS 6/60 OU Nasal step	OD 26 OS 26	OU—0.125% qd	OD 22 OS 24	0	None	
B.N. 75-C-F	O.A.?	OU-P 4%, Es 1% qid Aceta 125 mg qid	None	OD 5°–10° OS none	OD 26–34 OS 26–34	OU—0.25% bs	OD 26 OS 28	0		Grade 2 diabetic retinopathy
O.T. 61-C-M	O.A.	OU-P 3%, Es 1% qid Aceta 125 mg qid	OD Iridencleisis OS Trephine	OD 4/60 OS 3/60 Advanced loss to 20 mm object	OD 33 OS 66	OU—0.25% bid Aceta 125 mg bid	OD 18.5 OS 22	+	None	
M.T. 70-C-F	O.A.	OS-P 4%, Es 1% qid Aceta 125 mg qid	OS None	OD no LP OS 6/60 OS 5°–8° with 10 mm object	OD <7 OS 26–30	OS—0.125% bid Aceta 125 mg qid	OD <7 OS 22	+	None	OD Post-operative prolonged choroidal detachment with iris prolapses
W.T. 65-W-M	O.A.	OU-P 4%, Es 1% qid Aceta 250 mg qid	None	OD none OS 2/60 End stage field	OD 26–36 OS 19–30	OU—0.25% bid Aceta 250 mg qid	OD 26 OS 26	0	None	Erratic tensions for years. Doubtful if patient uses any medication faithfully
J.W. 70-C-M	O.A.	OS-P 4%, Es 1% qid Aceta 125 mg qid	OD Iridencleisis	OD End stage OS Full to 1/1000	OS 19–33 Average 26	OS—0.25% bid Aceta 125 mg qid	OS 26	0	None	
T.S. 50-C-F	O.A.	OU-P 3%, Es 1%	OU Trephine 1953	OU 20°	OD 19 OS 22	OU—0.25% bid	OD 22 OS 22	+	None	Controlled on previous medication also
D.B. 50-C-M	Aphakic	OS-P 4%, qid Aceta 250 mg qd	OS Cataract extraction with V touching cornea	OD 6/9 OS 1/60 OS 5° field	OS 26	OS—0.25% qd	OS 16	+	None	OS Endo-epithelial dystrophy. Cataract secondary to trauma age 5 yr.
H.B. 47-C-F	Salzmann's nodular dystrophy	OU-P 4%, Es 1% qid Aceta 250 mg bid	Before surgery	OD 6/60 OS 6/60 5° fields	OD 36 OS 26	OU—0.25% bid	OD 60 OS 36	—	Pain	Also on Aceta 125 mg. qid.
	Secondary to phlyctenular keratitis	OU-DFP .1%, Epineph 2%	OU Scheie procedure	Same	Unable to tolerate DFP	OU—0.25% bid	OD 40 OS 40	0	None	Excellent control with echothiophate iodide plus epinephrine bitartrate 2%, tension OU26. Patient stopped epinephrine bitartrate because of burning
			OU Iridencleisis			OU—0.25% bid Epineph 2% bid	OD 26 OS 22	+		
C.F. 30-C-M	OS Epithelial downgrowth	OS-P 4%, Es 1% qid Aceta 250 mg qid	OS Cataract extraction	OD 6/4.5 OS 1/60 OD full fields	OS 36	OS—0.25% bid	OS 40	0	None	Also on Aceta 250 mg. qid.
A.H. 79-C-F	Aphakic	OU-DFP 0.05% qd	OU Iridectomy	OD 6/21 OS 6/21 OD 15° OS 5°	OU 22	OU—0.25% bid	OU 22	+	None	Patient didn't like DFP. Diabetes
E.M. 46-C-F	Uveitis	OU-P 3%, Es .5% qid	None	OD 1/60 OS 1/60	OD 36 OS 36	OU—0.25% bid	OD 22 OS 26	+	None	OU sublexated lenses OS macular hole

in a 30-year-old Negro who had had surgery several years earlier for a congenital cataract. Twenty of the 24 patients were Negro, with males and females about equally divided.

Type of glaucoma. Chronic simple open-angle glaucoma was the diagnosis in 19 of the 24 cases. The remaining cases included one patient whose angle was not classified because of an opaque cornea, one with glaucoma secondary to epithelial downgrowth, two due to peripheral anterior synechias following cataract surgery and one with glaucoma secondary to prolonged uveitis.

Previous medication. Before placing these patients on echothiophate iodide, they usually were using pilocarpine (four percent), eserine (one percent) and acetazolamide (250 mg.), all taken four times a day. Surgery, of course, was suggested concomitantly with each increase in dosage. Demecarium bromide was not used in this series. Two patients had been on isoflurophate but, because of intolerance on the part of one and dislike of the vehicle by another, it was stopped. Side-effects to acetazolamide were minor and infrequent. Although it has been stated that therapy with acetazolamide cannot be continued for a prolonged period, we find that, in the Negro clinic patients, if it is the only way a tension can be controlled and surgery is refused, 125 mg. (and often 250 mg.) four times a day will be tolerated with no complaints for years, without calculi formation, skin eruptions, loss of appetite or other side-effects. One patient in this series volunteered that tingling of her extremities was caused by the acetazolamide (250 mg. q.i.d.) but this was relieved by decreasing the dose to 125 mg. q.i.d.

Previous surgical procedures. Eleven of the 24 patients (20 of 43 eyes) had had some form of glaucoma procedure in the past: three Scheie glaucoma operations (peripheral iridectomy with scleral cautery), 11 iridencleisis operations, two iridectomies and four Elliot trephining procedures. In our hands, tension control in Negroes has been achieved most frequently by the trephining or scleral punch procedures, followed by iridencleisis, and least often by a peripheral iridectomy with scleral cautery. Surgery on Negroes has not been as rewarding as in Caucasians. Five eyes were aphakic.

Vision and fields. Most of these cases showed a marked loss of field in addition to a high incidence of poor visual acuity.

Previous tension and tension on echothiophate iodide. Tensions were taken with a Schiøtz tonometer using the 7.5-gm. weight and the 1955 scale. Patients were seen every two to four weeks.

Echothiophate iodide dose and frequency. The initial dose was 0.25-percent echothiophate iodide at night. If this proved too strong, it was reduced to 0.125 percent. Only one patient in this group was unable to take the medication and another stopped only because the degree of miosis was impairing her vision. We attempted to decrease the frequency of dosage but, in this series, most patients had to take the drops at least once a day, usually at night, and often twice a day. The drugs most frequently used in conjunction with echothiophate iodide were epinephrine bitartrate (two percent) and acetazolamide.

Efficacy of ecothiophate iodide. If the tension was controlled with echothiophate iodide, or remained under control after change from a previously effective medication, a "plus" was recorded, if uncontrolled a "zero," and if the tension increased a "minus."

Of 43 eyes, there were 35 in which a tension of 25 mm. Hg or higher was present despite vigorous treatment with eserine, pilocarpine and acetazolamide. Tensions of 25 mm. Hg or less were noted in 20 of these eyes (57 percent) when echothiophate iodide was used supplemented in several cases with 1-epinephrine bitartrate (two percent), acetazolamide or both. Two patients (four percent) suffered a rise in tension with echo-

thiophate iodide. One rise was minor and responded to a change in medication. This patient was a Negress and her angle was reported as open, grade one. The second case, H. B., had a rather pronounced rise in tension but an advanced band-shaped keratopathy prevented classification of the angle. Later, she had a filtering procedure and was placed back on echothiophate iodide with good control.

Side-effects. No systemic side-effects, iris cysts, uveitis, retinal detachments or local allergic manifestations toward this drug occurred. Headaches, unless severe, are not noted but occurred routinely for the first two to three days on this medication.

Remarks. Five cases of diabetes (21 percent) are present in this hard-to-manage group. This series is too small for one to conclude that glaucoma in the diabetic bears a poor prognosis but it is something which merits watching. Occasionally excellent initial responses were noted with echothiophate iodide and later a relapse occurred. This is common with any drug in the treatment of glaucoma. Acetazolomide and l-epinephrine bitartrate (two percent) or both have proven useful adjuncts in glaucoma not responding satisfactorily to echothiophate alone.

Summary

The results are reported of the treatment with echothiophate iodide of 43 eyes of 24 patients suffering from glaucoma. All but two cases were previously uncontrollable with conventional medication. Intraocular pressure was controlled by echothiophate iodide in 57 percent of the eyes or 63 percent of the patients. These results are in satisfactory agreement with previous investigators[1-7] who have reported control in 38 to 86 percent of previously uncontrollable eyes, depending upon the criteria of response used for evaluation. It is felt that echothiophate iodide is particularly advantageous in the indigent clinic patient because (1) its less frequent administration gives greater likelihood that the eyedrops will actually be taken, and (2) it will control difficult cases where no other combination of conventional drugs has been effective. No side-effects of any consequence were observed.

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INTRAVENOUS UREA AND ANGLE-CLOSURE GLAUCOMA*

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INTRODUCTION

The treatment of patients with acute angle-closure glaucoma has always presented a problem. Diamox in combination with miotics was introduced in 1954[1] but, although this drug was a significant aid, a number of patients were refractory to it. Other carbonic anhydrase inhibitors offered no improvement over Diamox. Trying to break a hypertensive crisis by increasing aqueous outflow (miotics) and/or by decreasing inflow (carbonic anhydrase inhibitors) was not completely successful.

Osmotic therapy with intravenous sucrose has also been utilized[2] but its risks (renal toxicity[3]) and ineffectiveness left much to be desired. The high molecular weight made it necessary to administer huge doses of the drug in order to achieve a satisfactory osmotic gradient.

The recent reintroduction of urea into clinical ophthalmology seems to have lessened significantly the problems of treating intractable angle-closure glaucoma. Detailed studies of this osmotic agent have been carried out and its mode of action well defined.[4] Several clinical reports have commented on its use.[5-7] It is the purpose of this communication to report on the limitations and range of usefulness of intravenous urea in four patients with acute angle-closure glaucoma.

MATERIAL AND METHODS

Four patients with intractable angle-closure glaucoma were treated with intravenous urea on the Eye Service of the Long Island College Hospital. One patient required the drug for control of ocular tension in each eye and so five eyes are included in this study. None of the patients had responded to intensive miotic and Diamox therapy.

Intravenous urea was administered, as had been suggested,[5] in a dose of one gm. per kg. of weight as a 30-percent lyophilized solution in 10-percent invert sugar. The rate of flow was usually three to five cc. per minute, but was increased in those patients who demonstrated damage to the blood aqueous barrier (see comment).

CASE REPORTS

CASE 1

Mrs. R. McN., a 75-year-old white woman, was admitted to the Long Island Hospital with severe pain in the right eye and right-sided headache of 13 hours' duration. This was accompanied by persistent vomiting and rapid loss of vision in the right eye.

On admission, the right eye had a visual acuity of hand movements at two feet, and demonstrated marked congestion of the bulbar conjunctiva. The cornea was edematous, the anterior chamber extremely shallow and the pupil oval, fixed, and almost fully dilated. The intraocular pressure was 80 mm. Hg. The left eye was normal except for a shallow anterior chamber and a corrected visual acuity of 20/40 due to nuclear lens changes. Ocular tension was normal. Past history revealed treatment for hypertensive cardiovascular disease of 12 years' duration. In addition, three different attacks of myocardial infarction had occurred four, eight, and 12 years previously.

Medical therapy was instituted immediately consisting of 500 mg. of Diamox intravenously with Prostigmine (five percent) and Mecholyl (20 percent) solution, administered every 10 minutes in the right eye. Pilocarpine (two percent) was given prophylactically every two hours in the left eye. Demerol and Thorazine were injected intramuscularly for the control of pain and vomiting. After two hours of such therapy the ocular tension in the right eye was still 70 mm. Hg and the pupil had failed to constrict. At the end of the third hour on this same regime the tension in the right eye was 60 mm. Hg.

At this point urea was administered intravenously. The dosage was one gm. per kg. of weight in a solution of 10-percent invert sugar. Forty-five minutes later the ocular tension in the right eye

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was 8.0 mm. Hg. The patient was taken to the operating room where a single pillar iridencleisis was performed with excellent results.

A successful prophylactic peripheral iridectomy was carried out one week later on the left eye. At this time the corrected visual acuity in the right eye had improved to 20/70.

CASE 2

Mrs. D. G., a known hypertensive for 25 years and suffering from angina pectoris for eight years, was admitted to the Long Island College Hospital with an acute myocardial infarction. She had experienced intermittent attacks of pain in both eyes during the previous six months, with blurring of vision and redness of the right eye. One day after admission, she developed such an attack in the right eye with decrease in vision. The visual acuity could not be quantitated since the patient was confined to bed. On examination she appeared to have shallow anterior chambers in each eye with an oval semidilated pupil in the right eye. The tension was 35 mm. Hg in the right eye and 22 mm. Hg in the left eye. With miotic therapy the tension dropped to normal limits and surgery was deferred because of the recent myocardial infarction. The patient was discharged from the hospital five weeks following the attack of angle-closure glaucoma.

She had not been faithful in using her eye medication and so was readmitted to the hospital one month later with pain in her right eye accompanied by severe chest pain. Examination revealed marked congestion of the globe, edema of the cornea, a very shallow anterior chamber and moderate dilatation of the pupil. The tension measured 60 mm. Hg in the right eye. The visual acuity of the left eye was 20/70, anterior chamber shallow, and the pupil miotic. The eye was not congested but the tension was 31 mm. Hg. The intraocular pressure was controlled, using a combination of 500 mg. of Diamox given intravenously and topical Carcholin (1.5 percent).

Two days later, although on combined oral Diamox and local miotic therapy, the patient experienced pain in her left eye. The cornea appeared somewhat steamy with congestion of the globe. The pupil, however, was still miotic. The intraocular pressure, in spite of therapy, was 9.0 mm. Hg in the right eye and 60 mm. Hg in the left eye. Urea, 1.0 gm./kg. was given intravenously in 10-percent invert sugar and the pressure dropped within 45 minutes in both eyes to 4.0 mm. Hg.

The patient was scheduled for surgery, but this had to be deferred because of a recurrence of anginal chest pain. Profuse perspiration, a result of Carcholin toxicity, necessitated changing to Pilocarpine for continued miosis. When, in spite of medication, the pressure the next day was found to be 47 mm. Hg in the left eye, the same dosage of urea was repeated with a drop once again to 4.0 mm. in each eye. A one-pillar iridencleisis was performed immediately and five days later a similar procedure was carried out on the right eye. The patient made an uneventful recovery and ocular tension was controlled in both eyes thereafter without medication.

CASE 3

Miss K. B., a 43-year-old white woman, was admitted to the Long Island College Hospital because of a severe left-sided headache with pain in the left side of her face of three days' duration. These symptoms were accompanied by nausea, vomiting and marked diminution in vision of the left eye. No previous history of ocular symptoms was elicited except for poor vision in the right eye since childhood.

Visual acuity on admission was corrected to 20/300 in the right eye with a −5.0D. sph. The anterior chamber was moderately deep. The right eye was esotropic (15 degrees) and ocular tension was 22 mm. Hg. No other abnormalities in this eye were observed. The vision of the left eye was found correctible to 20/80 with a +3.5D. sph. and demonstrated deep perilimbal injection, a steamy cornea, a shallow anterior chamber and a dilated pupil refractory to light. The tension was 70 mm. Hg. and the fundus appeared to be normal.

Medical therapy was started immediately, consisting of Diamox, 500 mg. intravenously with Carcholin (1.5 percent) every 15 minutes in the left eye and prophylactically every four hours in the right eye. Demerol was given intramuscularly for pain and Compazine for the control of nausea and vomiting. Two hours later the tension was found to be unchanged and so urea (1.0 gm./kg.) was administered in a solution of 10-percent invert sugar. The pressure was still unchanged one and a half hours later and the miotics were changed to Prostigmine (five percent) and Mecholyl (20 percent) alternating every five minutes in the left eye. These drugs, too, failed to alter the pressure.

It was assumed that urea failed to lower the intraocular pressure because of damage to the blood aqueous barrier as a result of a three-day history of symptoms prior to medication. A satisfactory osmotic gradient, essential to lower the pressure, had not been obtained. Eight hours later, a second dose of intravenous urea (1.0 gm./kg. in 10-percent invert sugar) was administered in five minutes (instead of half an hour) with the patient outside the operating room. With this very rapid administration, a satisfactory osmotic gradient was obtained and the pressure dropped to 18 mm. Hg in the left eye one-half hour later. The patient was moved immediately into the operating room where a complete iridectomy was performed.

Postoperatively, the tension in the left eye, as measured with the Goldmann applanation tonometer, remained in the 30's and could only be controlled with Diamox. Tonography showed a diminished facility of outflow. Three weeks after the initial iridectomy, a single pillar iridencleisis was performed, resulting in excellent control of the intraocular pressure for the past three months.

CASE 4

Mrs. I. P., a 51-year-old white woman with

known diabetes for 17 years and poorly controlled because of irregular diet habits and insulin administration, entered the Long Island College Hospital with severe pain in the left eye of three days' duration. The pain was accompanied by a left frontal headache and persistent vomiting. She had noticed a decrease in vision since the onset of symptoms. There had been no such episodes previously.

Visual acuity was 20/50 in the right eye and hand movements at one foot in the left eye. Examination revealed 4+ injection of the left globe with moderate edema of the cornea. The anterior chamber was deep in each eye with moderate rubeosis of the iris in the right eye and marked rubeosis in the left eye. Gonioscopic study demonstrated wide anterior chamber angles in each eye with neovascularization of the entire circumference of the trabecular meshwork in the left eye. The ocular tension was 23 mm. Hg in the right eye and 64 mm. Hg in the left eye.

Medical therapy, consisting of Diamox, Pilocarpine and Demerol, was instituted. The tension in the left eye dropped to 35 mm. Hg in several hours but failed to respond further. Humorsol (0.25 percent b.i.d.) and Epitrate (two percent) also failed to reduce the tension and two days later the pressure rose to 46 mm. Hg in the left eye. Urea was then given intravenously (1.0 gm./kg. in 10-percent invert sugar) at a rate of four cc. per minute. The pressure dropped to 27 mm. Hg 45 minutes later but failed to respond further. With continued Diamox and miotic therapy the tension was maintained at this level for several days, fluctuating in the low 30's. Two weeks later, a modified Scheie procedure was performed. An eight-mm. scleral incision was made into the anterior chamber with the Hildreth coagulator and a hole burned into the iris with the coagulator to effect an iridectomy. Postoperatively, a good filtering bleb formed and the tension was controlled.

Observations and Comment

A review of the cases just presented indicates that urea was an effective therapeutic agent for lowering the intraocular pressure in patients with acute angle-closure glaucoma who had not responded to a combination of miotic and Diamox therapy. It was most efficacious in the first three cases but not in the fourth. The first three were primary and the last a secondary angle-closure variety of glaucoma. This drug satisfies the prerequisites for an ideal osmotic agent. It has low molecular weight, is nontoxic, with poor ocular penetration, thus permitting the development of a high and sustained osmotic gradient. With this therapy the glaucomatous crisis can be broken and the patient prepared either for immediate surgery or controlled by miotics for surgery at a later date. The surgery is then performed under ideal conditions.

Limitations in the use of Diamox are apparent in Case 2, where an acute attack ensued in a patient under intensive Diamox and miotic therapy. The conscientious administration of miotics merely served to drain further an already shallow anterior chamber in an eye where Diamox had failed to break the crisis. In addition, flooding the conjunctival cul-de-sac with miotics produced symptoms of parasympathetic toxicity. All these factors served to cause a precipitous rise in pressure that was broken only by urea, thus effectively utilizing the osmotic principle. Surgery could then take place under ideal conditions.

The rate of flow of the intravenous urea, as has been mentioned, was three to five cc. per minute. At this rate the entire dosage (1.0 gm./kg. in 10-percent invert sugar) was delivered in 30 to 60 minutes. However, in one case it was necessary to administer a second dose in five minutes, when earlier urea had failed to produce hypotony of the globe. The patient had experienced symptoms of acute glaucoma for three days. Increased turbidity of the aqueous and damage to the blood aqueous barrier, a result of neglect, altered the osmotic reqirements. Rapid administration of urea, however, served suddenly and effectively to increase the osmotic gradient to a point where the drug could exert its effect in the presence of a turbid aqueous and a severely damaged blood aqueour barrier.

The limitations of urea's usefulness are most apparent in Case 4. Secondary glaucoma was present as a result of the proliferation of new blood vessels on the iris surface and in the anterior chamber angle. This neovascularization was due to diabetes mellitus of long duration. Intravenous urea, administered at a rapid rate, produced a moderate and short-lived fall in intraocular pressure. A turbid aqueous, the result of neovascularization,

coupled with a broken aqueous barrier, made it impossible for urea to produce a high and sustained osmotic gradient. In this instance, therefore, urea was of limited value.

The one side-effect noted was occasional headache. This was attributed to a fall in the cerebrospinal fluid pressure of short duration.[4]

Summary

Intravenous administration of urea produced a rapid fall in the intraocular pressure in three out of four patients with acute angle-closure glaucoma, who had been refractory to a combination of Diamox and miotic therapy.

The drug has only limited usefulness in patients with secondary glaucoma who demonstrate a turbid aqueous and damage to the blood aqueous barrier. Establishing a satisfactory osmotic gradient is thus prevented.

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THE ACTION OF UREA IN ACUTE GLAUCOMA*

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There are few events in ophthalmology as dramatic as the precipitous drop in intraocular pressure which follows the use of urea in acute glaucoma. This occurs within 45 minutes, regardless of etiology, and despite the failure of previous therapy. The measurable effect of intravenous urea lasts five to 12 hours. Although initially it was suggested only in the management of acute glaucoma in preparation for surgery, it has become apparent that the boundaries of its usefulness reach beyond this limitation. In angle-closure glaucoma, urea, by its rapid lowering of intraocular pressure, enables miotics to become effective and terminates the acute attack. Operative management then becomes elective, with iridectomy the procedure of choice.

Urea is a substance of broad scientific interest which, until recently, has been therapeutically neglected. Historically, urea is important as the first organic substance to be synthesized from inorganic compounds (Fredrich Wohler in 1828) thereby initiating the field of organic chemistry.

Phylogenetically, it is the chief end-product of protein metabolism in mammals, as differentiated from birds and reptiles, which excrete uric acid, presumably to conserve water.

Physiologically, by acting as a carrier, it detoxifies the NH_3 resulting from deamination during metabolism of amino acids. It is formed in the liver from arginine, carried in the blood stream, and excreted by the kidney by glomerular filtration. Fifty percent is reabsorbed by the kidney tubules by an active

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secretory mechanism. There is an obligatory loss of large volumes of water caused by the osmotic effect of unabsorbed urea. It is freely diffusible into tissue fluids, with the exception of aqueous humor and cerebrospinal fluid. Urea is not utilized in nutrition. At least 25 percent is hydrolyzed in the alimentary tract by intestinal bacteria; this can be prevented by oral administration of neomycin.[1]

Urea in the reduction of intraocular pressure was first used in animals intravenously by Hertel[2] in 1917, and intraperitoneally by Fremont-Smith[3] in 1927. Javid,[4] in 1956, evaluated urea clinically in the form of a 30-percent solution dissolved in 10-percent invert sugar suitable for intravenous use, and found it remarkably effective in reducing intracranial pressure. In 1958,[4] he reported its use in ophthalmology in cases of acute glaucoma in preparation for surgery, in retinal detachments, and in orbital exploration. Galin, Aizawa, and McLean,[5] in 1959, presented a series of cases of acute glaucoma of various etiologies and confirmed the effectiveness of urea. In a recent report,[6] they have stressed its use in inducing hypotony in angle-closure glaucoma, which often permits miotics to exert their effect and mechanically open the angle.

The use of hypertonic solutions in the therapy of glaucoma is not new. Sucrose, glucose, sorbital and saline have all been used with varying success. However, because of transient effect and rapid excretion, their routine use was discontinued. Urea fills the need for a reliable hypertonic agent. It is a physiologic substance handled constantly by the kidney in amounts up to 30 gm. daily. Its low molecular weight and poor ocular diffusibility contribute toward its effectiveness. The reabsorption by the kidney prolongs its action. Although a diuretic, urea acts mainly by an osmotic effect. Clinically, the reduction in intraocular pressure occurs before diuresis. The lowering of cerebrospinal fluid pressure and presumably intraocular pressure is enhanced in nephrectomized animals.[7] The osmotic pressure of the blood is at its maximum at the time of greatest reduction in intraocular pressure.[5]

In terms of the secretion diffusion theory of aqueous humor formation, the aqueous is hypertonic to the plasma, and remains so through an active metabolic process, with the secretions of ions by the ciliary epithelium. There is a net flow of water from plasma to aqueous depending on the osmotic gradient. The concept of osmotic transport has recently been questioned.[8-10] With administration of urea, there is an increase is osmolarity of the plasma, with a consequent reduction in osmotic gradient, and reduction in the formation of aqueous humor. The magnitude of this effect as well as simultaneous determination of plasma and aqueous osmotic pressures during urea administration have yet to be determined. Acetazolamide (Diamox) has been shown to reduce the formation of aqueous humor by approximately 50 percent in the absence of osmotic changes.[11] However, the rapid fall in intraocular pressure with the use of urea in the presence of a completely closed angle, in cases unresponsive to Diamox, apparently involves more than inhibition of aqueous humor formation.

Theoretically, it would appear that a reversed osmotic gradient occurs, with a net outflow of fluid from the intraocular structures to the plasma, with dehydration of aqueous, vitreous and perhaps other intraocular tissues. This net diffusional outflow may occur at such sites as the ciliary epithelium, the epithelium and capillaries of the iris, and the internal limiting membrane of the retina. Experimentally Bering and Avman[12] have shown that changes in intracranial pressure are dependent on an osmotic pressure gradient between serum and cerebrospinal fluid. As long as the osmotic pressure of serum was greater than that of the cerebrospinal fluid, the intracranial pressure fell but, as the serum and cerebrospinal fluid came into osmotic equilibrium, the fall in pressure stopped. When the pressure of cerebrospinal fluid became greater than that

of the serum, the intracranial pressure began to rise. It would seem reasonable to assume a similar mechanism in effect between serum and aqueous humor.

The dosage of urea used intravenously was 1.0 gm. per kg., dissolved in 10-percent invert sugar and administered at a rate of 4.0 cc. per minute, in cases resistant to Diamox and miotics. Reduction in pressure occurred within 45 minutes and the pupils became miotic. In those cases in which pupillary constriction occurs with urea therapy, despite ineffectiveness of previous medical measures, it is a most favorable prognostic sign. All patients were maintained subsequently only on pilocarpine. Iridectomy was performed later as an elective procedure and was effective in controlling the tension in these cases.

The observation that miosis occurs following the reduction of pressure supports the concept that previous unresponsiveness to miotics was due to sphincter paralysis. Tyner and Scheie[13] have demonstrated experimentally that a critical level of increased intraocular pressure occurs at which the pupil dilates, no longer responds to miotics and will not constrict until the pressure is lowered. In animal eyes in which both sympathetic and parasympathetic denervation was performed at various levels, a rise in intraocular pressure, with the use of saline injection into the vitreous, caused dilatation of the pupil when the pressure was above 60 mm. Hg, despite the previous use of pilocarpine. Additional miotics had no effect until the pressure was reduced and then pupillary constriction occurred. They have placed the disturbance at the level of the sphincter muscle cell, caused by depression of function due to increased intraocular pressure. An alternate explanation is impairment of the vascular supply to the sphincter muscle by compression, in view of sector atrophy of the iris following acute attacks.

Urea therapy is well tolerated. Moderate headache has been a common complaint in all patients. It resembles the headache following lumbar puncture and is due to a similar mechanism, reduction in intracranial pressure. The headache responds to the usual analgesics and bedrest. The intravenous needle should be well placed since local tissue infiltration causes discomfort and may result in necrosis. Moderate chills, lasting five minutes with no temperature elevation, occurred in one patient.

Although caution is advised in administering urea to patients with renal disease, moderate elevation in BUN is not a contraindication. The signs of uremia are not due to elevation of urea but to other toxic substances due to poor kidney function, of which elevated urea levels are an indication. Recently, Grollman and Grollman[14] have ascribed toxicity directly to urea alone in animals at plasma levels of 370 to 480 mg. percent by intraperitoneal lavage. In patients, therapeutic levels of urea rarely reach 150 mg. percent and return to normal within one or two days.

Murphy and co-workers[15] have called attention to the marked excretion of sodium which may occur in patients given intravenous urea following major surgery. Since it is not uncommon for angle-closure glaucoma attacks to occur during this period, electrolyte studies may be indicated in such patients treated with urea to avoid hyponatremia.

By its osmotic property, urea increases blood volume. Bounous and co-workers[16] have demonstrated in animals that rapid injection of urea may increase blood volume as much as 30 percent. In patients with diminished cardiac reserve, this may prove hazardous. Acute pulmonary edema was precipitated in Case 3 near the completion of the infusion and lasted 30 minutes. It responded to conservative treatment but was undoubtedly improved by the rapid diuretic action of urea—a welcomed safety mechanism. On another occasion, when urea was administered slowly to the same patient over a period of 75 minutes, there were no complications. It is suggested that cardiac and hypertensive patients be observed carefully during the in-

fusion and that it be given at a slower rate. Blood volume studies are being undertaken to determine the extent of these factors.

Report of cases

Case 1

F. R., a 75-year-old woman was admitted to Montefiore Hospital for acute glaucoma, O.D., of seven hours' duration. There had been one episode of pain, O.D., several months previously, which had subsided spontaneously. The right eye was markedly congested, with corneal edema and a fixed dilated pupil. Intraocular pressure was 94 mm. Hg, O.D.; 18 mm. Hg, O.S. Treatment with pilocarpine, eserine, and intravenous Diamox reduced the tension to: O.D., 76 mm. Hg, over a five-hour period. The pupil remained fixed. Intravenous urea and pilocarpine reduced the tension within 45 minutes to 12 mm. Hg and the pupil became miotic. The patient was maintained on pilocarpine. Gonioscopy demonstrated an open angle while on miotics. Six days later an iridectomy was performed. Examination over a period of one year has revealed normal tension in both eyes.

Case 2

J. S., a 69-year-old man was admitted for acute angle-closure glaucoma of 24 hours' duration. There had been no previous episodes. Intraocular pressure was 50 mm. Hg in a painful, congested left eye, with corneal edema. There was no response to miotics or intravenous Diamox over a four-hour period. Intravenous urea was administered, with pilocarpine instilled locally. After 35 minutes, the tension was 18 mm. Hg and the pupil was constricted. The patient was maintained on pilocarpine locally. Gonioscopy disclosed an intermediate angle. A peripheral iridectomy was performed, O.S., the next day. The tension has remained normal after six months.

Case 3

R. C., a 69-year-old woman, was admitted to Montefiore Hospital for acute angle-closure glaucoma, O.S. Six years previously, iridencleisis was performed elsewhere for acute glaucoma, O.D. The patient had been maintained on pilocarpine in both eyes but, because of elevation of base pressure, was also given phospholine iodide in the left eye by her referring physician. Each of two instillations was followed by pain, browache and headache. On the day of admission, there was blurring and diminution of vision, with severe headache. The patient was a known cardiac patient with hypertension. She was receiving digitalis therapy. Systemic examination was unremarkable except for a loud Grade 3 systolic murmur. Examination disclosed a filtering iridencleisis and dense cataract, O.D. The left eye was severely congested; corneal edema was present. The pupil was small, irregular, and measured two mm. Tension was 90 mm. Hg, O.S., and 15 mm. Hg, O.D. There was no response to pilocarpine and intravenous Diamox.

Urea was given intravenously, with local instillation of pilocarpine. Within 30 minutes the tension was 21 mm. Hg, O.S., and the pupil became round and smaller. Toward the completion of therapy the patient became dyspneic and developed acute pulmonary edema. The infusion was discontinued. Coarse, moist rales were present bilaterally. The condition was improved by elevating the patient to the sitting position. Morphine sulfate was administered. The attack subsided and the lungs were clear after 30 minutes. The patient was maintained on pilocarpine. The pupils remained pinpoint in size. Subsequent examination revealed a visual acuity of hand movements, O.D.; 20/30, O.S. Gonioscopy disclosed a partially closed angle and broad bands of synechias. The patient refused surgery and was discharged.

Two months later she was readmitted for acute glaucoma of the same eye while using pilocarpine. The tension of 69 mm. Hg was reduced to normal with intravenous urea, given slowly over a 75-minute period. There were no systemic effects other than headache. The pupil became miotic. Iridectomy was performed three days later.

Case 4

W. K., a 71-year-old man, was admitted for bilateral acute angle-closure glaucoma. The patient had a suspected intraocular tumor, O.D., and dilatation with 10-percent Neosynephrine had induced bilateral acute glaucoma. Previous gonioscopy by his referring physician had disclosed an intermediate angle, O.U. There was congestion and corneal edema of both eyes, with the pupils dilated and fixed. Intraocular pressure was 46 mm. Hg, O.D., and 59 mm. Hg, O.S. There was no response to pilocarpine and intravenous Diamox over a four-hour period. Intravenous urea was given with local instillation of pilocarpine and within 45 minutes the tension was 15 mm. Hg, O.U. The pupils became miotic. Iridectomy was performed, O.D., two days later.

Subsequent examination revealed a solid discolored elevation above the macular region. P^{32} uptake was positive in the suspected area. The eye was enucleated and pathologic examination confirmed the diagnosis of malignant melanoma. Microscopically, the anterior chamber angle was open with no synechias present. The trabeculae appeared normal.

Case 5

E. H., a 64-year-old woman, was admitted because of acute glaucoma, O.S., of 24 hours' duration. There was a history of halos around lights but no pain. One day prior to admission, the patient developed severe headache, diminution of vision, nausea and vomiting. Examination disclosed a congested, painful eye with a fixed dilated pupil. Tension was 80 mm. Hg, O.S. There was no response to Diamox and pilocarpine over a three-hour

period. Intravenous urea was given, with pilocarpine instilled locally. Within 45 minutes the tension was 25 mm. Hg and the pupil became miotic and more regular. Subsequent tensions were 12 mm. Hg, O.D., and 8.0 mm. Hg, O.S. Gonioscopy revealed a narrow angle with no synechias. An iridectomy was performed the following day.

CASE 6

E. K., a 67-year-old woman, was admitted because of acute angle-closure glaucoma, O.D., of one day's duration while on pilocarpine. The left eye was sightless from a severe glaucoma attack 14 years previously. There was no response to Diamox, eserine, and pilocarpine. On admission, the cornea was edematous, the chamber shallow, and the pupil small. Intraocular pressure was 64 mm. Hg. With intravenous urea and pilocarpine instilled locally, the pressure was lowered to 15 mm. Hg. The pupil became pinpoint in size. Subsequent studies revealed a narrow but open angle. Iridectomy was performed three days after admission.

CASE 7

R. B., a 67-year-old woman, was admitted because of acute angle-closure glaucoma, O.D., of two days' duration while on pilocarpine. An acute attack in the same eye three weeks previously had been successfully treated with Diamox and pilocarpine. The patient refused surgery and was discharged. Two days before the second admission there was recurrent pain and blurring of vision, O.D. At admission, intraocular pressure was 50 mm. Hg. The eye was severely congested with corneal edema. The pupil was dilated and fixed. There was no response to intravenous Diamox, eserine, and pilocarpine. Intravenous urea was administered and the tension was reduced to 12 mm. Hg within 25 minutes. The pupil became miotic and eccentric. Subsequent studies revealed a narrow angle which was functioning and iris atrophy. An uneventful iridectomy was performed three days later.

SUMMARY

1. Intravenous urea dramatically lowers intraocular pressure in acute angle-closure glaucoma resistant to other medical therapy.

2. Miosis, when occurring, is a favorable prognostic sign and indicates the termination of the attack. Patients can then be maintained on miotics.

3. Iridectomy, as an elective procedure, was the operation of choice in such cases.

4. Acute pulmonary edema was precipitated in one case by urea therapy.

5. The mechanism of action of urea is discussed.

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PIGMENTARY GLAUCOMA

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For many years the significance of primary pigment accumulations in the anterior part of the eye has been the subject of clinical analysis. In some cases efforts were made to interpret the appearance of such pigment on the posterior surface of the cornea, anterior part of the iris, capsule of the lens, or the zonular fibers of the vitreous body, in others attempts were made to connect these pigment accumulations with glaucoma. Since Krukenberg (1899) first observed spindle-shaped pigmented spots on the posterior surface of the cornea, a number of authors have reported their observations (Stock, 1901; Thompson-Ballantyne, 1903; Mills, 1913; Koeppe, 1916; Krupa, 1917; Hansen, 1918; Massmann, 1920; Vogt, 1921; Jess, 1923). Of these, Koeppe, Hansen and Jess were the first to connect pigment either on the cornea or the iris with glaucoma and they emphasized the problem of the clinical microscopic picture of pigmentary glaucoma. Vogt considered this corneal pigmentation to be a phenomenon of senility and gave no special clinical interpretation. He also thought there was no connection between this corneal pigmentation and glaucoma.

Of all these authors, however, Koeppe (1916) was most interested in establishing some connection between glaucoma and the changes observed by Krukenberg and pigmentation of the iris. He studied 64 cases of simple glaucoma and was able to establish pigmentation of the cornea, iris or ciliary body. Koeppe found microscopically that such cases showed disintegration of the pigment epithelial cells and partial disintegration of the pigment polyedrical cells. Koeppe considered these findings extremely important in primary glaucoma. In further studies he was able to establish almost without exception that such findings were present either before or after the onset of simple glaucoma. He likewise stressed that suspected glaucoma cases may be detected biomicroscopically by glaucomatous pigment changes at a time when other symptoms of glaucoma have not yet become manifest. He sought the cause of formation of this pigment in the sympathetic system and mentions neurotrophic disturbances in the iris epithelium, linking these changes with the observation of heterochromia of the iris.

Hansen further established after death, in a case of long-standing glaucoma in a patient aged 68 years, microscopic pigmented pinpoint cells on the posterior surface of the cornea and in the canal of Schlemm, as well as pronounced accumulations of pigment on the posterior surface of the iris. In the nonglaucomatous left eye of the same patient, there were no pigmentary changes. Hansen further observed a deposit of pigment on the posterior surface of the cornea in cases of diabetes mellitus. He interpreted this finding as diabetic degeneration of the posterior layer of the iris. In such cases there is swelling of tissue of the iris and deposits of glycogen, with disintegration of the pigment cells. Pigment is then transported by the aqueous humor to the posterior surface of the cornea.

It was already known at that time that pigmentation could be detected microscopically in nonglaucomatous cases (Hansen), and Vogt stated that pigmentation is no more frequent in persons suffering from glaucoma than in elderly subjects not suffering from

glaucoma. Long before these reports Hippel (1901) was of the opinion that glaucoma was due to obstruction of the chamber angle by pigment. In 1908, Levinson established microscopically in glaucoma infiltration of the chamber angle by pigment grains. He thought they originated from the posterior epithelial layer of the iris.

In 1923, Jess also raised the question of pigmentary glaucoma. In the left eye of a glaucoma patient aged 64 years, he established depigmentation of the pupillary edge, as well as corneal pigmentation and pigment grains in the vitreous humor, in the iris near the chamber angle and in the anterior capsule of the lens. This finding verifies Jess' diagnosis of pigmentary glaucoma in the left eye. He further stressed that pigment accumulations in the anterior part of the eye were significant in some cases of glaucoma.

Strebel and Steiner (1915) mention the existence of corneal pigmentation in four cases of high myopia, while Kraupa (1917) records six such cases which he called melanosis endothelialis corneae. Kayser (1919) records one case of bilateral megalocornea with Krukenberg's symptom. This patient was 23 years of age; examination in his 15th year had revealed no pigment in the cornea. Both eyes recorded slight myopia of 2.75D. Koby (1917) reported annular pigmentation of the area around the equator of the lens and Zentmayer described a case of pigmentation of the capsule of the lens in which there was corneal pigmentation after Krukenberg.

During the first period of clinical and microscopic description of simple pigmentary glaucoma, the greatest credit is due Koeppe who correlated the presence of pigment on the posterior surface of the cornea and the anterior surface of the iris with the occurrence of glaucoma. In cases where such pigmentation existed but in which the symptoms of increased intraocular pressure were not yet manifest, Koeppe diagnosed preglaucoma for, in such cases, increased intraocular pressure occurred sooner or later.

In more recent times Sugar (1940) mentioned finding pigment in the corneal angle in one case of chronic glaucoma. In another report Sugar and Barbour (1949) mention cases of pigmentary glaucoma in which the chamber angle is unobstructed but there is extensive pigmentation of the scleral trabeculae. The Krukenberg corneal symptom was established in all six cases and irritation of the anterior part of the eye in two cases. Most of the cases reported by Sugar and Barbour were in young persons with glaucoma pigmentosum.

Calhoun (1953) reports six cases of this disease at ages varying from 23 to 27 years. Riffenburg reports one case (1953) of a 21-year-old youth with a corneal pigment spindle and all the other symptoms of pigmentary glaucoma.

Somewhat earlier (1941) Evans, Odom and Wenaas presented a statistical review of 107 cases with Krukenberg's corneal pigment taken from the literature, as well as a review of 95 cases of their own. In only 12 cases was there glaucoma of the juvenile type, including six considered as pigmentary glaucoma.

In 1957, Bick reported five cases with Krukenberg's spindle and symptoms of glaucoma pigmentosum. In all five cases the scleral trabeculae were pigmented. Bick especially stresses the value of transillumination of the iris in cases of pigmentary glaucoma. It is possible in this manner to establish depigmentation of the iris, as pointed out by Koeppe.

In 1956, Malbran reported seven cases in young persons, aged 20 to 30 years, in whom he observed Krukenberg's spindle with symptoms of pigmentary glaucoma. In three of these there was megalocornea; this led him to believe that these were cases of congenital glaucoma.

According to Gorin and Posner (1957) it is not yet possible to distinguish between the pathologic finding of pigmentary grains in the trabeculae and sclera in glaucoma, as this finding occurs in normal persons, as well.

François (1955) detected pigmentations in the chamber angle in 71 percent of cases of simple glaucoma and in 64 percent of normal persons over the age of 50 years. Out of 122 persons who were normal Beuningen (1959) established pigmentation of the chamber angle in 16 cases.

Scheie and Fleischauer (1958) presented a report on the examination of 49 patients (97 eyes) for idiopathic atrophy of the epithelial layer of the iris and ciliary body. They found Krukenberg's spindle in 92 of the 97 eyes. In pigmentation of the trabeculae they found various degrees of affliction: in 65 cases grade IV, in 25 grade III and in two cases slight pigmentation. Transillumination revealed atrophy of the iris in a number of cases. In all cases they were able to establish pigmentation of the posterior capsule of the lens, while in 12 eyes there was a complete peripheral pigmentary ring on the lens. In 21 cases (42 eyes) Scheie and Fleischauer established glaucoma and in these cases the pigmentation of the trabeculae was much more marked. In other cases observed, although the pigmentation was more marked, no glaucoma could be established. However, these authors also mention that such cases must be checked for possible glaucoma.

As a further contribution to the clinical picture of pigmentary glaucoma, one must mention Etienne and Pommier (1957) and Etienne (1959). In his paper on glaucoma pigmentosum, Etienne describes his 12 patients ranging in age from 10 to 63 years (six men and six women). In 10 of these patients Krukenberg spindles were established. There was also pigmentation of the trabeculae and atrophy of the iris. In nine of these cases pigmentary glaucoma was diagnosed.

Reporting on his three cases, Beuningen mentions that pigmentary glaucoma may be divided into the juvenile and senile type. In studying 420 cases of simple glaucoma, he established an extensive pigmentation of the chamber angle in 54 cases. He considered that these pigmentations became more marked in cases of simple glaucoma of long duration.

As already mentioned, glaucoma is more frequent in women and myopia of a higher or lower degree is encountered in this form of glaucoma. Krukenberg's spindle is usually found in pigmentary glaucoma, as well as the changes in pigmentation in the other parts of the anterior eye already mentioned. Gonioscopy and tonography are of great importance in the examination of such eyes. These examinations could not be carried out by the older authors.

Transillumination, which Koeppe first used in cases of pigmentary glaucoma, was often used, especially by Scheie, Fleischauer, Bick and Etienne. In the cases which I observed tonography and gonioscopy were carried out regularly, while in cases in which the intraocular pressure was not marked provocative tests with caffein-priscol were done. In individual cases the water test, compression of the jugular veins and tests involving the usual mydriatics were done. Special attention was given to transillumination, not only of the iris but also of the ciliary body. This test is essential in those cases in which there may be atrophic changes of the ciliary body.

In interpreting the gonioscopic findings, an endeavor was made to have them as exact as possible. The findings on the intensity of pigmentation in the chamber angle were divided into three groups: (1) slight pigmentation of the trabeculae, (2) medium pigmentation in which the line of pigmentation was always continuous, and (3) extensive pigmentation in the whole trabecular area right up to the annulus of Schwalbe. An attempt was made in cases in group 1 to discard those which had only a few pigmented spots. These spots had to be visible in the area of the canal of Schlemm or all over the trabecular meshwork. Only a few pigmented dots were considered normal; in elderly persons they may be due to senile and atrophic phenomena in the pigmented

layer of the iris or ciliary body which are without visible changes.

Transillumination was carried out in every case as an essential part of the examination. This method should always be applied, not only in cases of glaucoma but in all other cases where atrophy of the iris and ciliary body is suspected. In addition to the usual transillumination after Koeppe in the area of the iris, attention was given to transillumination of the ciliary body for which the cone of a diascleral lamp should be set as far behind the equator of the sclera as possible in order to visualize the shadowing of the area of the ciliary body. In a normal ciliary body one can see diffuse shadowing of a radius of about six mm. while the pericorneal zone is somewhat lighter. In cases in which there is atrophy of the pigmented layer of the ciliary body one can see, in the normally shadowed ciliary sphere, lighter sectors which, in some cases, partially or totally cover the circumference.

The patients in whom Krukenberg spindles were observed were divided into two groups: (1) patients with Krukenberg spindles, both elderly and young, who had myopia of varying degrees; (2) patients with congenital eye anomalies who, apart from other ocular symptoms, had Krukenberg corneal spindles.

Series I. With and without glaucoma

Case 1

P. S., aged 54 years, was examined in the outpatient clinic from March 11 to 14, 1955. Both eyes showed the Krukenberg spindles with minute spots, as well as incipient peripheral cataracts. Vision was R.E., 6/6?; L.E., 6/6?. Intraocular pressure was: R.E., 20 mm. Hg; L.E., 19 mm. Hg. Provocation with priscol-caffein showed: R.E., 22 mm. Hg; L.E., 22 mm. Hg. Tonography: R.E., C = 0.024; L.E., C = 0.051. Blood pressure 150/100 mm. Hg.

Gonioscopy. The trabeculæ in both eyes showed medium pigmentation, the chamber angle was open; there were no other pathologic findings. In the central part of the iris an annular atrophy 1.5 mm. in diameter was seen by transillumination. The ciliary body showed no changes.

Case 2

R. M., aged 49 years, was examined in the outpatient clinic from June 16th to 18th. Both corneas showed Krukenberg spindles with minute spots. Other findings were normal. Transillumination showed in both eyes a slight but continuous annular atrophy of the iris one mm. in width and several radial atrophic spots. Other findings normal. Vision was: R.E., 6/10, with a +1.5D. sph. 6/6; L.E., 6/10, with a +1.25D. sph. 6/6. Intraocular pressure was: R.E., 21 mm. Hg; L.E., 22 mm. Hg. Tonography: R.E., C = 0.053; L.E., C = 0.053. Provocation with priscol-caffein yielded the same tension in both eyes.

Gonioscopy. The trabeculae showed slight pigmentation; other findings were normal.

Case 3

M. I., aged 52 years, was examined in the outpatient clinic from November 10 to 12, 1956. In both corneas were Krukenberg spindles with minute spots. Transillumination of the iris showed atrophy at the edge of the sphincter and in the center of the iris. Other findings were normal. Vision was R.E., 6/12, with a +2.0D. sph. 6/6?; L.E., 6/15-6/12, with a +2.0D. sph. ×6/6?. Intraocular pressure was: R.E., 18 mm. Hg; L.E., 20 mm. Hg. Tonography: R.E., C = 0.052; L.E., C = 0.032. Provocation with priscol-caffein, 20 mm. Hg, O.U.

Gonioscopy. The trabeculae showed medium pigmentation.

Case 4

A. P., aged 28 years, was treated in March, 1956. Both corneas showed Krukenberg spindles with small spots of pigmentation on the iris and on the anterior lens capsule. Maximum mydriasis of the pupil showed no visible pigmentation in the area of the equator of the lens and on the zonular fibers. There were opacities of the vitreous body in both eyes. The fundus of both eyes showed a wide temporal myopic conus and atrophic myopic central chorioretinitis. Transillumination showed normal findings in both eyes.

Vision was: R.E., 2.5/60, with a −17D. sph., 6/24; L.E., 2.5/60 with a −16D. sph., 6/24. Intraocular pressure was: 18 mm. Hg, O.U. Tonography: C = 0.052, O.U. Provocation with priscol-caffein showed 21 mm. Hg in both eyes.

Gonioscopy. The trabeculae were more pigmented, while the other findings were normal. Transillumination showed a slight atrophy of the iris in both eyes.

Case 5

E. H., aged 58 years, was examined in the outpatient clinic in October, 1957. There was a Krukenberg spindle in both corneas. Multiple flocculi iridis were present on the pupillary edge of the iris in the left eye. On the anterior lens capsule of both eyes there were dotted pigmentations. The retina in both eyes showed senile degeneration of the macula lutea.

There was a central scotoma in both eyes. Vision without correction was 6/60, O.U. Intraocular pressure was: R.E., 20 mm. Hg; L.E., 18 mm.

Hg. Provocation with caffein-priscol: R.E., 32 mm. Hg; L.E., 20 mm. Hg. Tonography: R.E., C = 0.15; L.E., C = 0.24.

Gonioscopy showed medium pigmentation of the trabeculae. Transillumination of the iris showed slight atrophy. The findings on the ciliary body were normal.

CASE 6

M. S., aged 82 years, was examined in April, 1957. There was an incipient senile cataract in both eyes and a Krukenberg spindle in both corneas. The retinal blood vessels showed medium arteriosclerotic changes. Uncorrected vision was: R.E., 1/60; L.E., 1/60. Intraocular pressure: O.U., 30 mm. Hg. Tonography: O.U., C = 0.63. Provocation with priscol-caffein: R.E., 35 mm. Hg; L.E., 38 mm. Hg.

Gonioscopy showed slight pigmentation of the trabeculae in both eyes. Transillumination showed atrophy of the iris. The ciliary body was normal.

CASE 7

V. V., aged 68 years, when examined in October, 1957, showed Krukenberg spindles in both corneas and incipient opacities in both lenses. The vitreous in both eyes had dustlike opacities. Vision was: R.E., 6/10, with a +1.0D. sph., 6/6?; L.E., 6/8, with a +1.0D. sph. 6/6?. Intraocular pressure: R.E., 20 mm. Hg; L.E., 25 mm. Hg. Provocative test: R.E.. 26 mm. Hg; L.E., 32 mm. Hg. Tonography: R.E., C = 0.024; L.E., C = 0.095.

Gonioscopy showed pigmentations of the trabeculae in both eyes of medium intensity. Transillumination showed atrophy of the iris in both eyes between the 10- and 3-o'clock positions, while the ciliary body transilluminated more between the 11- and 2-o'clock positions.

CASE 8

M. S., 70 years of age, was examined in July, 1958. There were Krukenberg spindles in both corneas and tiny dotted pigmentations on the anterior capsule of the lens. Both eyes showed a temporal myopic conus. In the right eye there was a glaucomatous excavation of the papilla. Vision was: R.E., 1/60, with a −6.0D. sph., 5/60; L.E., 6/60, with a −3.0D. sph., 6/6. Intraocular pressure: R.E., 40 mm. Hg; L.E., 20 mm. Hg. Tonography: R.E., C = 0.12; L.E., C = 0.024. Provocative test: R.E., 48 mm. Hg; L.E., 28 mm. Hg.

Gonioscopy in the right eye showed the trabeculae to be more pigmented; the pigmentations were less marked in the left eye. Transillumination of the iris showed slight atrophy in both eyes. The ciliary body showed more marked transillumination nasally and upward in both eyes.

CASE 9

K. D., 48 years of age, was examined in June, 1958. The Krukenberg spindles were more marked in the cornea of the left than of the right eye. On the anterior capsule of the lens minute pigmentations were seen in both eyes. Other findings were normal. Vision was: R.E., 6/7-6/8; L.E., 6/7-6/6. Intraocular pressure: R.E., 26 mm. Hg; L.E., 55 mm. Hg. Tonography: R.E., C = 0.092; L.E., C = 0.022.

Gonioscopy showed pigmentation of the trabeculae of medium intensity in both eyes. Transillumination of the iris showed slight atrophy and translucency of the ciliary body more marked upward in both eyes.

CASE 10

M. K., 60 years of age, was examined in October, 1958. There were Krukenberg spindles in both eyes. In the right eye was an incipient senile cataract, in the left, aphakia and dystrophy of the cornea (postoperative). Uncorrected vision was: R.E., 1.5/60; L.E., 1.5/60. Intraocular pressure was 7.5/30 mm. Hg, O.U. Tonography: C = 0.048, O.U. The provocative test: R.E., 40 mm. Hg; L.E., 44 mm. Hg.

Gonioscopy showed slight pigmentation of the trabeculae in both eyes. Transillumination of the iris showed a continuous atrophy of slight degree in both eyes. The ciliary body also showed atrophic changes upward, temporally and nasally.

CASE 11

S. M., aged 58 years, was examined in November, 1958. Complicated cataract was present in the right eye and a Krukenberg spindle in the left eye, as well as incipient senile cataract. Vision was: R.E., amaurosis, L.E., 5/60, with a −1.0D. ⌒ −2.0D cyl. ax. 120°, 6/24. Intraocular pressure: R.E., 10 mm. Hg; L.E., 25 mm. Hg. A provocative test with priscol-caffein: R.E., 10 mm. Hg; L.E., 36 mm. Hg. Tonography: L.E., C = 0.16.

Gonioscopy showed medium pigmentation of the trabeculae. Transillumination showed a slow continuous atrophy throughout the middle portion of the iris and of the ciliary body.

CASE 12

P. E., aged 47 years, was examined in November, 1958. In the right eye was a Krukenberg spindle with minute spots; in the left eye this finding was less marked. Dotted pigmentation was present on the anterior capsule of the lens and pigment dotted the iris of both eyes. There were small floating opacities in the vitreous of both eyes. Vision was: 6/15, O.U. Intraocular pressure: 26 mm. Hg, O.U. Provocative test: R.E., 30 mm. Hg; L.E., 32 mm. Hg.

Gonioscopy showed medium pigmentation of the trabeculae. Transillumination showed slight atrophy of the iris; the ciliary body was normal.

CASE 13

M. M., aged 30 years, was examined in December, 1958. Krukenberg spindles were present in both eyes. In the right eye was a total cataract; in the left eye there were opacities in the vitreous body, atrophic myopia and central choroiditis. Vision was: R.E., projection of light at six m.; L.E.,

2/60, with a −15.0D. sph., 4.5/60. Intraocular pressure: R.E., 18 mm. Hg; L.E., 19 mm. Hg. Provocative test: 22 mm. Hg, O.U. Tonography: O.U., C = 0.051.

Gonioscopy showed pigmentation of the trabeculae of medium intensity in both eyes. Transillumination showed slight atrophy of the iris and ciliary body in both eyes.

CASE 14

R. D., aged 58 years, was examined in January, 1959. In the right eye the findings were normal. In the left eye there were Krukenberg spindles and pigmented spots on the anterior capsule of the lens. Atrophy of the iris was more marked in the left eye. There was a glaucomatous excavation of the papilla on the left eye (figs. 1 and 2). Vision was: R.E., 6/6; L.E., amaurosis. Intraocular pressure: R.E., 25 mm. Hg; L.E., 50 mm. Hg. Tonography: R.E., C = 0.024; L.E., C = 0.033.

Gonioscopy showed slight pigmentation of the trabeculae in the right eye, more marked in the left eye. Transillumination showed medium atrophy of the iris in the right eye and very marked iris atrophy in the left eye. Atrophy of the ciliary body by transillumination was more marked on the left side. The left eye was enucleated in March, 1959.

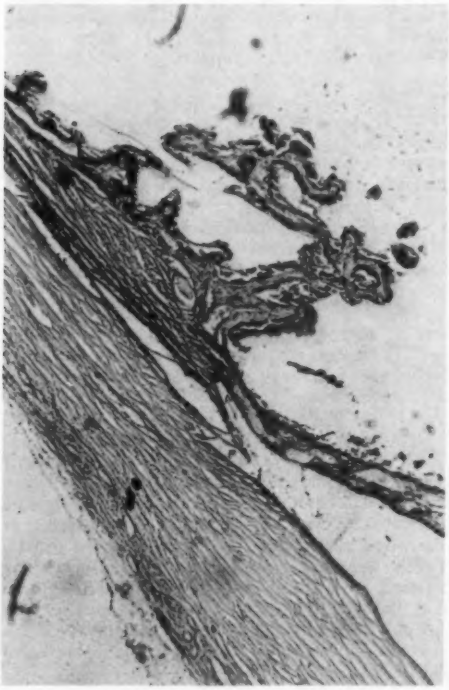

Fig. 1 (Čavka). *Case 14,* Series I. Pigmented granules in the angle of the anterior chamber. (Hematoxylin-eosin, ×100.)

Fig. 2 (Čavka). *Case 14,* Series I. Very intensly pigmented angle of the anterior chamber and atrophic structure of the ciliary body. (Hematoxylin-eosin, ×600.)

CASE 15

R. N., aged 57 years was examined in April, 1959. There were Krukenberg spindles in both eyes and pigmented spots on both irises. The irises also showed atrophy and their pupillary edges were more pigmented. There were pigmented spots on the anterior capsule of the lens in both eyes. A glaucomatous excavation was present in the left eye. Vision was: R.E., 6/6; L.E., 6/24 (s.c.). Intraocular pressure: R.E., 20 mm. Hg; L.E., 45 mm. Hg. Provocative test of the right eye gave 22 mm. Hg. Tonography: R.E., C = 0.019; L.E., C = 0.027.

Gonioscopy showed medium pigmentation of the trabeculae in both eyes. Transillumination showed medium atrophy of the iris and ciliary body, more marked in the left eye than in the right.

CASE 16

P. S., aged 62 years, was examined in March, 1959. There was a Krukenberg spindle in the right eye. The iris showed an atrophic structure. Slight pigmentations were present on the anterior capsule, as well as total cataract. No pigmentations were seen in the left eye, although there was an incipient cataract in the left eye. Vision was: R.E., projection of light at six m.; L.E., 6/60. Intraocular pressure: R.E., 48 mm. Hg; L.E., 18 mm. Hg. After provocation test: R.E., 58 mm. Hg; L.E., 24 mm. Hg. Tonography: R.E., C = 0.085; L.E., C = 0.020.

Gonioscopy showed pigmentation of the trabeculae of medium intensity but less marked in the left eye. Transillumination showed circumferential atrophy of the iris and ciliary body in the right eye, less marked in the left.

CASE 17

B. V., aged 65 years, was examined in May, 1959. There were Krukenberg spindles and atrophic irises in both eyes, as well as incipient cataracts. Uncorrected vision was: O.U., 6/60. Intraocular pressure: R.E., 50 mm. Hg; L.E., 23 mm. Hg; Tonography: R.E., C = 0.085; L.E., C = 0.022.

Gonioscopy showed marked pigmentation of the trabeculae, more marked in the right than in the left eye. Transillumination showed medium atrophy of the iris.

CASE 18

V. V., aged 16 years, was examined in June, 1959. There were Krukenberg spindles in both eyes and opacities of the vitreous body with myopic changes in the fundus of both eyes, more marked on the left side. Vision was: R.E., 2/60, with a —0.0D. sph., 6/30; L.E., 0.5/60, with a —16.0D. sph., 3/60. Intraocular pressure: O.U., 20 mm. Hg. Following provocation test: O.U., 22 mm. Hg.

Gonioscopy showed slight pigmentation of the trabeculae in both eyes. Transillumination was normal.

CASE 19

D. S., aged 57 years, was examined in July, 1959. There were bilateral Krukenberg spindles and atrophic structure of the iris, predominantly in the left eye. Glaucomatous excavation of the papilla was present on the left side. Vision was: R.E., 6/15, with a —1.0D. sph., 6/12; L.E., projection of light at 25 cm. Intraocular pressure: R.E., 16 mm. Hg; L.E., 40 mm. Hg. After provocative test: R.E., 20 mm. Hg; L.E., 50 mm. Hg. Tonography: O.S., C = 0.065.

Gonioscopy showed medium pigmentation of the trabeculae of the left eye, marked pigmentation of the right eye.

Transillumination of the iris showed a marked atrophy on the left side, circumferential and continuous; on the right, it was partial in the upper sector. On the right side the ciliary body showed normal transillumination, while on the left side there were atrophic changes along the whole circumference in diameter about three mm.

CASE 20

V. K., aged 63 years, was examined in September, 1959. There were bilateral Krukenberg spindles of the cornea and bilateral incipient senile cataract. Vision was: R.E., 5/60; L.E., 2/60. Intraocular pressure was: R.E., 20 mm. Hg; L.E., 18 mm. Hg. After provocative test: R.E., 22 mm. Hg; L.E., 21 mm. Hg.

Gonioscopy showed slight pigmentation of the trabeculae and transillumination of the iris and ciliary body was normal in both eyes.

CASE 21

H. D., aged 27 years, was examined in November, 1959. There were bilateral Krukenberg spindles of the cornea. Vision was: R.E., 5/60, with a +2.75D. sph., 6/6?; L.E., 5/60, with a —3.0D. sph., 6/6?. Intraocular pressure: O.U., 23 mm. Hg. After provocative test: R.E., 30 mm. Hg; L.E., 28 mm. Hg. Tonography: R.E., C = 0.048; L.E., C = 0.078.

Gonioscopy showed slight pigmentation of the trabeculae in both eyes. Transillumination of the iris and ciliary body was normal in both eyes.

CASE 22

S. M_h, aged 54 years, was examined in December, 1959. Incomplete Krukenberg spindles were present in both eyes. In the iris of both eyes were marked accumulations of pigment in the form of islands and there were pigmented dots on the anterior lens capsule in both eyes. Vision was: O.U., 6/60, with a +1.0D. sph., 6/18. Intraocular pressure: O.U., 30 mm. Hg. After provocative test: O.U., 38 mm. Hg. Tonography: R.E., C = 0.17; L.E., C = 0.13.

Gonioscopy showed bilateral pigmentation of the trabeculae of moderate degree. Transillumination showed radial atrophy of the iris in both eyes. The ciliary body was normal.

CASE 23

M. D., aged 46 years, was examined in December, 1959. Incomplete Krukenberg spindles were present in both eyes, as were senile cataracts and atrophic structure of the iris. Vision was: R.E., 2/60, with a —18.0D. sph., 6/6; L.E., 0.5/60, with a —16.0D. sph., 4.5/60. Intraocular pressure, O.U., 20 mm. Hg. After provocative test: R.E., 28 mm. Hg; L.E., 23 mm. Hg. Tonography: O.U., C = 0.29.

Gonioscopy showed pigmentation of the trabeculae more marked on the right than on the left. Transillumination revealed atrophy along the upper edge of the iris in both eyes. The ciliary body was normal.

CASE 24

B. Lj., aged 54 years, was examined in December, 1959. Bilateral Krukenberg spindles were marked and dotted pigmentations were on the anterior capsules of both lenses. In the left eye there was glaucomatous excavation of the papilla. Vision was: R.E., 6/6; L.E., 6/18; Intraocular pressure was: R.E., 23 mm. Hg; L.E., 38 mm. Hg. Tonography: R.E., C = 0.20; L.E., C = 0.10.

Gonioscopy showed medium pigmentation of the trabeculae in both eyes. Transillumination revealed annular atrophy of the iris in both eyes.

CASE 25

M. R., aged 60 years, was examined in December, 1959. There were bilateral Krukenberg spindles.

In the right eye was an incipient senile cataract; in the left, operative aphakia, leukoma corneae with secondary degenerative changes. Vision was: R.E., 1/60, not correctible; L.E., 0.5/60, not correctible. Intraocular pressure: R.E., 32 mm. Hg; L.E., 30 mm. Hg. After provocative test: R.E., 42; L.E., 40 mm. Hg. Tonography: R.E., C = 0.075; L.E., C = 0.10.

Gonioscopy showed bilateral moderate pigmentation of the trabeculae. Transillumination showed annular atrophy of the iris in both eyes.

Comment

In this short review (table 1) of cases it can be seen that there were bilateral Krukenberg corneal spindles in 23 cases; in two cases, they were unilateral. A complete Krukenberg spindle was found in 20 cases; in five cases it was incomplete, that is, less marked. In 18 cases there was simple glaucoma and in seven the intraocular pressure was normal even after the provocative test, which means that there were no symptoms of glaucoma. Marked pigmentation of the iris existed in four cases, while pigmentation on the anterior lens capsule was established in eight cases. These pigmentations were formed into small spots and did not give the impression of the remnants of a persistent pupillary membrane.

Gonioscopy revealed slight pigmentation of the trabeculae in eight cases, medium pigmentation in 13 cases and marked pigmentation in four. Transillumination of the iris showed an atrophy of greater or lesser degree in 22 cases, while the ciliary body showed atrophic changes in only seven cases. There was myopia in seven cases, hypermetropia in four cases and emetropia in three cases. In three cases there was high myopia and in the remaining four cases there was myopia of a lower degree.

Krukenberg spindles and other eye symptoms existed in elderly persons in 21 cases; in only four cases did the patients' ages vary from 16 to 30 years. These symptoms were detected in the fifth decade of life in four patients, in the sixth decade in 11, in the seventh decade in five, and in the ninth decade in one patient.

Series II. With congenital anomalies of the eye

In contrast to the cases in Series I in which it was observed that the Krukenberg spindles existed in elderly persons in whom there were no congenital anomalies, in the eye or any other part of the body, in Series II will be presented cases with pigmentation in the anterior segment of the eye in which at the same time there were congenital changes in the eye.

Case 1

R. Z., aged 40 years, was examined in January, 1959. There were bilateral Krukenberg spindles and megalocornea, in the right eye measuring 13 mm. in both diameters, and in the left eye, 12.5 mm. Ectropion of the uveal pigment was present on the pupillary edge of both eyes and there was clearly visible dustlike pigment in the iris of both eyes. Dustlike pigment could be seen on the anterior capsule of the left lens and on the anterior hyaloid membrane of the right eye. In the right eye there was postoperative aphakia and in the left eye a complete cataract. A myopic conus and central degenerative myopic changes were present in the right eye. Vision was: R.E., 1.5/60, with a −6.0D. sph., 6/12; L.E., projection of light at six m. Intraocular pressure: R.E., 28 mm. Hg; L.E., 30 mm. Hg. After provocative test: R.E., 35 mm. Hg; L.E., 38

TABLE 1

Review of cases in Series I

Krukenberg Corneal Spindle (No. cases)	Pigmentation		Pigmentation of Trabecular Area		IOP Increased (No. cases)	IOP Increased with Provocative Test (No. cases)	IOP Not Increased (No. cases)
	Iris (No. cases)	Lens Capsule (No. cases)	Degree	Cases			
Bilateral in 23 Unilateral in 2	4	8	I II III	8 15 2	13	5	7

mm. Hg. Tonography: R.E., C = 0.22; L.E., C = 0.28.

Gonioscopy showed the chamber angle to be intensely pigmented in the trabecular area in both eyes. Transillumination of the iris showed radial lighter spots in both eyes; the ciliary body was normal. Radiography of the head and spinal vertebrae was normal.

CASE 2

A. S., aged 41 years, was examined in January, 1959. Bilateral Krukenberg spindles were present. The megalocornea of the right eye had diameters of 12.5 and 12 mm.; of the left eye, 12.5 and 13 mm. There were dotted pigmentations on the anterior capsule of the lens in both eyes and opacities of the vitreous body in both eyes. In both eyes there were circumpapillary atrophy of the choroid and central myopic changes of the chorioretina. Vision was: R.E., 2.5/60, with a −13D. sph., 6/18; L.E., 1/60, with a −15D. sph., 6/24. Intraocular pressure: R.E., 22 mm. Hg; L.E., 24 mm. Hg. After provocative test: R.E., 32 mm. Hg; L.E., 35 mm. Hg. Tonography: R.E., C = 0.49; L.E., C = 0.7.

Gonioscopy showed pigmentations of medium intensity in the trabeculae of both eyes. Transillumination showed a circular atrophy of the iris of 1.5 mm. The ciliary body was normal. Radiography of the head was normal.

CASE 3

I. S., aged 38 years, was examined in August, 1957 and checked in January, 1960. There was hydrophthalmos of both eyes with marked Krukenberg spindles in both corneas. The diameter of the right cornea measured 13 mm., of the left, 14 mm. The pupillary edge showed bilateral depigmentations and incipient cataract. Numerous pigmented dots were present on the anterior capsule of the lens, apparently they were congenital. There was bilateral glaucomatous excavation of the papilla. Vision was: R.E., 6/30, with a +1.0D. sph., 6/10; L.E., 6/18, with a +0.5 D. sph., 6/10 to 6/8. Intraocular pressure: R.E., 50 mm. Hg; L.E., 40 mm. Hg. Tonography: R.E., C = 0.25; L.E., C = 0.10.

On July 25, 1957, the patient had an external cyclodiathermy with cyclodialysis (Čavka) of the right eye and an iridencleisis (Holth) of the left eye.

Gonioscopy showed partial obliteration of Schlemm's canal. There was marked bilateral pigmentation in the unobliterated part of the canal and in the rest of the trabecular area. Transillumination showed radial zones of pigmentation in the center of the iris and in the ciliary body of both eyes. Radiography of the head was normal.

CASE 4

G. M., aged 49 years, was examined in February, 1959. Bilateral megalocornea (12.5 by 13.5 mm.) and bilateral Krukenberg spindles were seen. Both irises showed slight atrophy. There were dotted pigmentations on the anterior lens capsule. There were bilateral incipient cataracts. Vision was: R.E., 2/60; L.E., 6/18. Intraocular pressure: O.U., 30 mm. Hg. After provocative test: R.E., 42 mm. Hg; L.E., 40 mm. Hg. Tonography: R.E., 0.08; L.E., 0.10.

Gonioscopy showed slight circular atrophy of the iris, 15 to 12 mm. in width, and in the area of the ciliary body. Radiography of the head and spine was normal.

CASE 5

H. M., aged 26 years, was examined in January, 1960. There was bilateral ectopia and coloboma of the lens and bilateral incipient powderlike opacities in the lens. Bilateral ectropion uveae was seen on the pupillary edge. Visible also was bilateral hernia of the vitreous body with dotted pigmentations in the lower aphakic part. In the right eye, in the nasal portion, were remains of a persistent pupillary membrane. Vision was: R.E., 0.75/60; L.E., 1/60. Intraocular pressure: O.U., 26 mm. Hg. After provocative test: O.U., 34 mm. Hg. Tonography: R.E., C = 0.20; L.E., C = 0.10.

Slight pigmentation of the trabeculae was present in both eyes. Transillumination gave normal findings. Radiography of the head, spine and limbs was normal.

CASE 6

U. P., aged 32 years, was examined on January 8, 1960. Bilateral ectopia of the lens with incomplete Krukenberg spindles was seen in the left eye. Ectropion of the uvea was present in both eyes, more marked in the area of the pupillary edge. In the area of the visible vitreous body of the left eye were dotted pigmentations. There were bilateral dotted opacities of the lens. Vision was: R.E., 0.75; L.E., 1/60. Intraocular pressure: R.E., 22 mm. Hg; L.E., 18 mm. Hg. After provocative test: R.E., 40 mm. Hg; L.E., 33 mm. Hg. Tonography: R.E., C = 0.24; L.E., C = 0.18.

Gonioscopy revealed bilateral pigmentation of the trabeculae, less marked on the right, more marked on the left. Transillumination showed normal findings in both eyes. Radiography of the head, spine and limbs was normal.

CASE 7 (figs. 3, 4 and 5)

R. B., aged 15 years, was examined in January, 1960. There were bilateral Krukenberg spindles and incipient hydrophthalmos. The diameters of the corneas were 13 by 12.5 mm. Bilateral ectropion of the uvea was present on the pupillary edge. The iris of the right eye showed radial atrophy. A cataractous lens luxated downward into the vitreous of each eye. The fundi showed temporal atrophy of the papilla, more marked in the left eye. Vision was: R.E., 2/60, with a +11D. sph. +0.75D. cyl. ax. 90°, 6/36; L.E., projection of light at one m. Intraocular pressure: R.E., 30 mm. Hg; L.E., 26 mm. Hg. After provocative test: R.E., 38 mm. Hg; L.E., 34 mm. Hg. Tonography: R.E., C = 0.022; L.E., C = 0.087.

Gonioscopy showed goniosynechias and partial

obliteration of the angle and marked pigmentation of the trabeculae of both eyes. Transillumination showed atrophy of the right iris. The left iris was normal. Radiography of the head, spine and limbs was normal.

CASE 8

M. R., aged 24 years, was examined in December, 1959. Bilateral Krukenberg spindles and hydrophthalmos were seen. The diameter of the right cornea was 14 mm., of the left, 15 mm. Pigmentation dotted the anterior capsule of both lenses. Bilateral incipient atrophy of the papilla was seen. Uncorrected vision was: R.E., 1/60; L.E., 5/60. Intraocular pressure: O.U., 35 mm. Hg. Tonography: O.U., C = 0.14.

Gonioscopy: R.E., Grade II pigmentation; L.E., Grade I. The irises showed slight atrophy.

CASE 9

S. S., aged three years, was examined in January, 1959. There were incomplete bilateral corneal Krukenberg spindles. The megalocornea of the right eye measured 12.5 by 12.5 mm. in diameter, of the left eye 12.5 by 13 mm. One year ago the luxated lens was removed from the vitreous of the left eye. In the right eye there was ectropion uveae at the pupillary edge with slight atrophy of the iris in the upper part between the 11-o'clock and 1-o'clock positions. Depigmented whitish zones were seen in the iris; the remaining portion showed marked brown pigmentation. There were similar findings in the iris of the left eye. The left lens was luxated into the vitreous body. Intraocular pressure was: R.E., 30 mm. Hg; L.E., 38 mm. Hg.

Gonioscopy showed marked pigmentation of the trabeculae in both eyes. Schlemm's canal showed partial obliteration. Transillumination of the iris showed circular atrophy in both eyes. The ciliary body was normal. Radiography of the head and spine was normal.

CASE 10

V. D., aged 27 years, was examined in November, 1959. In 1956, the left eye had been enucleated because of injury; it was enlarged the same as the right eye in which there were pronounced Krukenberg spindles. The central macula, the cornea (diameter, 13 by 14 mm.) and globe were enlarged. Hydrophthalmos was present. The iris showed atrophy. The lens was completely opaque and luxated into the vitreous body. There were opacities of the vitreous body in the temporal region; in the lower portion there was extensive retinal detachment. Vision was normal projection of light and feeling light at six m. Intraocular pressure: R.E., 13 mm. Hg; after provocative test 18 mm. Hg. Tonography: R.E., C = 0.093.

Gonioscopy showed goniosynechias and partial obliteration of Schlemm's canal, with marked pigmentation of the trabeculae. Transillumination showed marked circular atrophy of the iris and ciliary body. Radioscopy of the head and spine was normal.

Fig. 3 (Čavka). *Case 7*, Series II. Incipient hydrophthalmos with corneal Krukenberg spindles of both eyes.

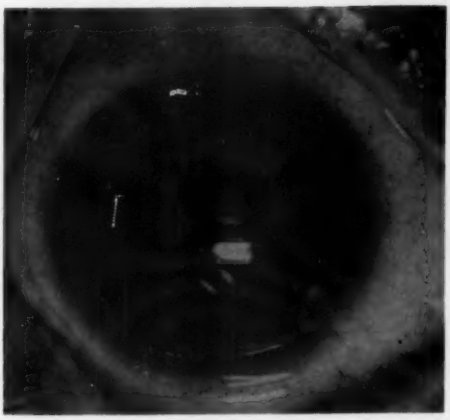

Fig. 4 (Čavka). *Case 7*, Series II. Atrophic structure of the iris of the right eye (hydrophthalmos).

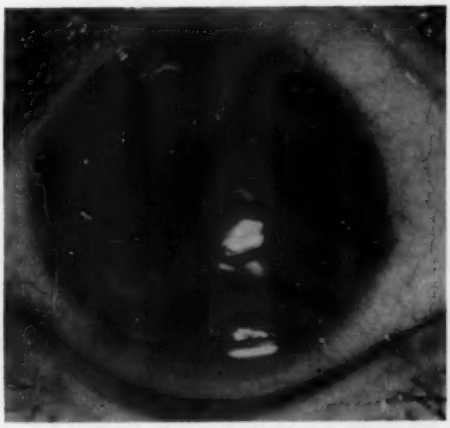

Fig. 5 (Čavka). *Case 7*, Series II. Slightly atrophic change in the iris of the left eye (hydrophthalmos).

CASE 11

J. M., aged 14 years, was examined in January, 1960. The patient suffered from dysostosis mandibulofacialis (Franceschetti-Zwahlen). On both microcorneas were marked small dotted Krukenberg spindles. Corneal diameters were seven and eight mm. The sclera of both eyes was thinned out and the pigment of the uvea shimmered through. Subcapsular opacities dotted both lenses. Other findings were normal in both eyes. Vision was: R.E., 5/60; L.E., 1/60. Intraocular pressure: R.E., 22 mm. Hg; L.E., 25 mm. Hg; after provocative test L.E., 35 mm. Hg. Tonography: R.E., C = 0.047; L.E., C = 0.16.

Gonioscopy showed medium pigmentation of the trabeculae in both eyes. Transillumination showed a slight radial atrophy of the iris. The patient also had bilateral congenital cataracts, hypotrichosis of the eyelashes and brows and irregular dentition. Radiography of the head, apart from the findings typical for this disease, was normal. Radiography of the spine and limbs was normal.

COMMENT (table 2)

In this series of 11 cases there were four cases (1, 2, 4 and 9) with bilateral megalocornea, two in men and two in women. The ages in three cases ranged from 40 to 49 years. Only in the one child, aged three years, (Case 9) was the megalocornea not complete; there were, however, several pigmented spots on the posterior surface of the cornea.

In three cases of megalocornea, the intraocular pressure was increased; in all four cases, pigmentation of the trabeculae was marked in both eyes. Transillumination showed iris atrophy in all four cases; in one, there was atrophy of the ciliary body as well. There was dotted pigmentation of the anterior capsule of the lens in three cases (1, 2 and 4), and there was ectropin uveae with congenital luxation of the lens in Case 9.

In addition to the four cases of megalocornea, there were four cases of hydrophthalmos in patients whose ages were 15, 24, 27 and 38 years, respectively, three of them women and one a man. In all four cases of hydrophthalmos there was a marked Krukenberg spindle. In three cases, the intraocular pressure was increased while in one case (9) there was hypotony due to extensive detachment of the retina. In these four cases, gonioscopy revealed marked pigmentation of the trabeculae and, in three cases (3, 8 and 10), transillumination showed marked atrophy of the iris and ciliary body; in one (7) there was only slight atrophy of the iris. In two cases (7 and 10), there was spontaneous luxation of the lens into the vitreous body.

It should be further mentioned that in this group there were two cases of congenital bilateral subluxation of the lens, in one case of which (fig. 5) there was no Krukenberg spindle, while in the other (fig. 6) there was an incomplete Krukenberg spindle in one eye.

In Case 5, there was congenital coloboma of the lens downward in both eyes. Although in Case 5 there was no Krukenberg spindle, there was visible dotted pigmentation in the lower aphakic portion in the vitreous body, which showed a prolapse into the pupillary space. Furthermore, there was ectropion uveae pigmentation of the trabeculae. Intraocular pressure was increased in both eyes. There were similar changes in Case 6 in the area of the vitreous body and chamber angle,

TABLE 2

REVIEW OF CASES IN SERIES II

Diagnosis	No. of Cases	Age (yr.)	Krukenberg Corneal Spindle (No. cases)	IOP Increased (No. cases)	IOP Not Increased (No. cases)
Megalocornea	4	1 case 3 3 in 50s	4	4	
Hydrophthalmos	4	15—38	4	3	1
Ectopia lentis	2	1 case 26 1 case 32	1	2	
Dysostosis Microcornea	1	14	1	1	

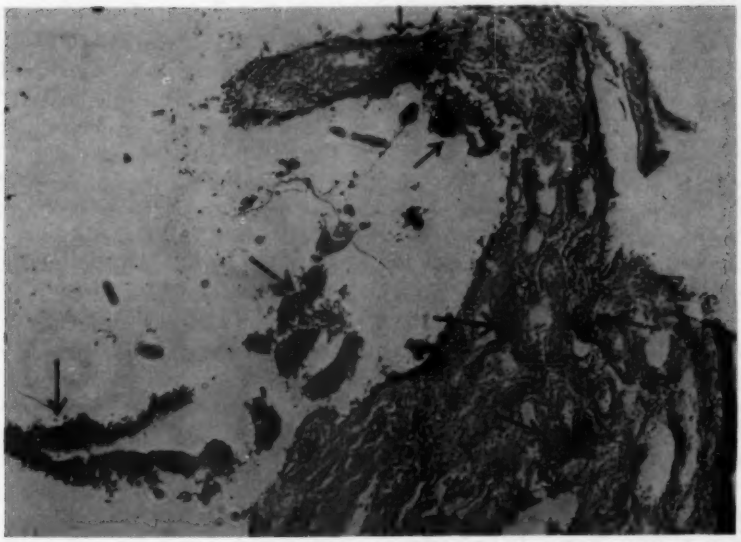

Fig. 6 (Čavka). A. S., aged 24 years, with complicated cataract, corneal Krukenberg spindles and secondary glaucoma of left eye. Very extensive pigmentation of the anterior layer of the iris with separation of the pigment spots. There are pigmented cells in the stroma of the iris, with intense pigmentation of the iris tissue. (Hematoxylin-eosin, ×400.)

together with increased intraocular pressure and pronounced ectropion uveae.

In this series of 11 cases—four of megalocornea, four of hydrophthalmos, and two of congenital ectopia of the lens and one of dysostosis mandibulofacialis, there was pathologic intraocular pressure in eight cases, and in three cases (Cases 2, 6 and 11) the intraocular pressure became increased and pathologic after provocation.

Discussion

In cases in which the symptoms favored the clinical picture of pigmentary glaucoma, the following symptomatology (as already mentioned to a certain extent by other authors—Koeppe, Jess, Sugar, Bick, Etienne and others): (1) Krukenberg corneal spindles; (2) pigmentation of the sclera and vascular emissaries of the sclera; (3) pigmentation of the iris and pupillary edge of the iris; (4) pigmentation of the lens capsule and the zonular fibers; (5) pigmentation of the chamber angle and chamber fluid; (6) pigmentation of the vitreous body; (7) increased intraocular pressure with or without the provocative test; (8) transillumination of the iris and ciliary body; (9) pigmentation in other parts of the eye (chorioretina and papilla of the optic nerve).

Naturally all these symptoms could not be established in all the cases; however, the clinical picture of pigmentary glaucoma was always accompanied by certain basic symptoms: pigmentation of the cornea, pigmented accumulations in the trabecular area and increased intraocular pressure.

A further analysis of the cases in Series I showed that there were 25 patients whose ages varied from 46 to 82 years in 21 cases, while four of the patients were in the second and third decade. In the 21 older patients who presented a symptomatology indicating pigmentary glaucoma, the pigmentary changes of the cornea, chamber angle, iris, ciliary body and lens capsule seemed most probably due to senile atrophic and degenerative changes of the pigmented layer of the iris and ciliary body. Consequently, these would be cases of decomposed pigment from

the pigment cells of the iris and ciliary body, transported by the chamber fluid to the posterior surface of the cornea and into the chamber angle or to the anterior surface of the iris, the lens capsule or zonular fibers. As already mentioned by other authors, beginning with Koeppe and until today, the accumulations of pigment in the area of the chamber angle and trabeculae play an important part in the occurrence of glaucoma. Consequently, the term of "acquired senile atrophic" should be applied to this form of pigmentary glaucoma.

The etiology remains vague in the four cases in which the patients were younger and showed either a high degree of myopia (three cases) or slight myopia (one case). The possibility in cases of high myopia, that the deposits of pigment in the cornea and chamber angle might be due to atrophic changes in the pigment layer of the iris and ciliary body should be considered.

Since all 11 patients in Series II showed congenital malformations of the eye—four megalocornea, four hydrophthalmos, two congenital ectopia of the crystalline lens and one of dysostosis mandibulofacialis—it is probable that the pigmentary glaucoma was also congenital. In Cases 5 and 6 with ectopia of the lens in both eyes, Krukenberg corneal spindles were not established in the left eye in Case 6 but such other symptoms as ectropion uveae, pigmentation of the vitreous body and trabeculae and increased intraocular pressure after the provocative test were present which led to the opinion that these cases should be classified as pigmentary glaucoma.

A survey of both series of cases is presented in Table 3 where one can see that, of the 36 patients observed, there was only one (congenital ectopia lentis Series II Case 5) in whom no Krukenberg spindle was present.

The intraocular pressure was normal in seven cases but, in the remaining 29 cases, it was increased bilaterally in 17 cases and unilaterally in 12 cases, making an increased intraocular pressure in 46 eyes or 64 percent of all the eyes examined. Of 97 eyes with the Krunkenberg spindle examined by Scheie and Fleischauer, glaucoma was found in 43.5 percent. Etienne established glaucoma in 18 eyes (75 percent) of 24 examined. Calhoun established glaucoma in six cases out of 11 with the Krukenberg spindle; in five the findings were negative. However, it has been known since Koeppe that there may be pigmentation of the anterior segment with no glaucoma, a condition which this author called preglaucoma. It is also known that pigmentation of the anterior segment are not only found in simple glaucoma but also in iris-block glaucoma (Koeppe). This author found 64 cases of simple glaucoma out of 70 cases, and only six of iris-block glaucoma acute or chronic. Both Sugar and Etienne established symptoms of iris-block glaucoma in two cases, while Malbran recorded three such cases, and Bick one. Observations so far favor the opinion that the number of cases of chronic simple glaucoma far exceeds that of congenital glaucoma.

These observations show that so-called pigmentary glaucoma may assume any of the clinical manifestations of other types of glaucoma—simple, iris-block, congenital, infan-

TABLE 3

ANALYSIS OF CASES IN BOTH SERIES I AND II

Krukenberg Corneal Spindle (No. cases)	Pigmentation of Trabecular Area		IOP Increased	IOP Not Increased	Refraction		
					Emetropia	Myopia	Hyperopia
	Degree	Casses					
Bilateral in 30	I	10					
Unilateral in 5	II	23	29	7	16	10	6
None in 1	III	3					

Transillumination of iris: in 28 cases atrophic changes.
Transillumination of ciliary body: in 10 cases atrophic changes.

tile and secondary. It is further shown that pigmentation of the cornea, iris and chamber angle are found in cases which show no glaucomatous symptoms. These findings make it difficult to classify this form of glaucoma.

It is difficult to say whether such cases can be spoken of as secondary glaucoma (Sugar, Etienne). Neither can one accept the opinion of Malbran that all cases of pigmentary glaucoma in which residua of the mesodermal chamber angle are found should be considered congenital. This can only be assumed in those cases in which there are not only congenital alterations in the chamber angle in the form of mesodermal residua but also megalocornea, hydrophthalmos and congenital heterochromia of the iris with hypertrophic pigmentation (Čavka).

It would also seem that the statement that persons suffering from pigmentary glaucoma are usually of a younger age, and that this disease is more frequent in women (Sugar, Malbran, Etienne) is incorrect, especially if one considers the observations of Scheie and Fleischauer who published a large number of cases in which the number of men was larger than the number of women, as well as my own study in which there is no great difference between the number of men (19) and women (17) patients and in which it is shown that pigmentary glaucoma can occur at any age. Other important symptoms play a significant part in the classification of this disease.

My study of cases of pigmentary glaucoma indicate that a separate entity for the clinical forms of this disease cannot be established and that the occurrence of pigment in the anterior sector of the eye must in most cases of primary glaucoma, be considered either accidental or a consequence of essential atrophy of the iris and ciliary body, or of atrophy due to other causes. Not only does this essential atrophy of the iris appear in middle and old age but also in infants and children.

In this connection we must stress the cases of infantile glaucoma (Series II, Cases 7, 8, 9 and 10) in which there were visible atrophic changes in the iris and depigmented areas on the anterior surface of the iris. The same applies to the cases of myopia (Series I, Cases 4, 8, 11, 13 and 23) in which transillumination showed atrophy of the iris and ciliary body: of eight cases of myopia, there were normal findings by transillumination in only two cases. Accordingly, in cases of infantile glaucoma as well as in those of myopia, the development of pigment in the anterior sector of the eye can be considered due to atrophic changes in the iris and ciliary body. Furthermore, in our cases with myopia no traces of congenital tissue were found in the chamber angle. Bick also mentioned that depigmentation of the iris in myopia might be considered analogous to chorioretinal atrophy of the posterior pole in myopia.

Beuningen tried to make a clinical classification of pigmentary glaucoma and divided pigmentary primary glaucoma into juvenile and senile forms. He further lists a secondary pigmentary glaucoma as occurring after iritis, contusions of the globe and in diabetes. I am of the opinion that this classification does not correspond to the actual clinical findings in pigmentary glaucoma, especially if one takes into consideration all the cases of pigmentary glaucoma published so far.

Since it has already been established that pigment can appear in the anterior segment of the eye not only in all forms of primary glaucoma but also in healthy persons, I am inclined toward a clinical classification of primary glaucoma into cases with visible pigmentation of the cornea and iris, in the chamber angle and so forth and those with no such symptoms. My opinion is supported by cases of healthy persons without glaucoma but with pigmentation of the anterior segment of the eye. It would seem that pigment is not an essential factor for the occurrence of glaucoma but that there must be other extraocular and ocular factors conditioning the occurrence of any form of primary glaucoma.

For these reasons it would perhaps be better to use the term "pigmentiforme" in all

cases of primary glaucoma in which there is pigmentation of the anterior segment of the eye, that is, iris-block glaucoma pigmentiforme, simple glaucoma pigmentiforme, infantile glaucoma pigmentiforme. Since pigmentation of the anterior segment of the eye can also occur in secondary glaucoma, in these cases, too, one might apply the term secondary glaucoma pigmentiforme.

On the basis of observations made so far on pigmentary glaucoma, it cannot be maintained that in cases of acquired forms of glaucoma, the deposits of pigment in the anterior segment of the eye, especially in the trabecular area, are the cause of increased intraocular pressure (glaucoma). As already pointed out it is my opinion that in various clinical forms of primary glaucoma, the appearance of pigment in the anterior segment of the eye is an accidental symptom and that the pigment is only one of many agents which further the development of primary glaucoma. This is the reason why I apply the term simple glaucoma pigmentiforme in cases of primary forms of glaucoma in which there is pigmentation, and not pigmentary glaucoma. I have endeavored in this way to subordinate the pathophysiologic appearance of pigmentation to the other symptomatology and agents of primary glaucoma.

Summary

In 36 patients symptoms of pigmentary glaucoma were established. In 35 cases there were Krukenberg corneal spindles; only in one case with ectopia lentis congenita was there no Krukenberg spindle. Of these cases 19 were in men and 17 in women. In 12 cases the patients were in the fourth decade of life; 26 patients were in the older decades.

Increased intraocular pressure was established in 46 eyes (64 percent of the eyes examined) while the trabeculae of the chamber angle were in all cases covered with more or less pigmentation.

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CORNEAL DYSTROPHY AND PARAPROTEINEMIA*

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A large number of corneal dystrophies have already been described, for the most part hereditary ones. One could mention, for instance, among the isolated parenchymatous degenerative conditions of the cornea, the congenital dystrophies: Groenouw's granular dystrophy, Haab-Dimmer's lattice dystrophy, Fehr's macular dystrophy, Schnyder's crystalline dystrophy, François' cloudy central dystrophy, lipoid degeneration, Vogt's cornea farinata, Maeder and Danis' deep filiform dystrophy.

Among the degenerative conditions of the limiting membranes should be mentioned Meesmann's epithelial dystrophy, Kraupa's epithelial dystrophy, Bücklers' annular dystrophy, Fleischer's whirling dystrophy, Vogt's mosaic degeneration, band-shaped corneal degeneration, posterior polymorphous degeneration, cornea guttata and Fuchs' endothelial dystrophy.

There are also the corneal dystrophies associated with thesaurismosis, such as gargoylism or Hurler's multiple dysostosis, François' dermo-chondro-corneal dystrophy, Hand-Schueller-Christian disease and cystinosis.

We had the occasion to observe a case of corneal dystrophy in which the morphology was quite unlike any other known type and which was associated with a paraproteinemia. It was, in fact, a diffuse myelomatosis, which shows very clearly the relationship between corneal dystrophy and disorders of protein synthesis and the protein composition of the blood.

Para- or dysproteinemias include Waldenström's essential macroglobulinemia, cryoglobulinemia (presence of a cold precipitable protein in the serum), Waldenström's hyperglobulinemic purpura and multiple myelomatosis.

The retinal signs are common and well known in dysproteinemia: slowing of retinal circulation, swollen and irregular veins, widespread hemorrhages, woolly or small punctate exudates, "exudative" detachment of the retina.

Other ocular signs are much rarer: hemorrhagic stains in the thickness of the iris stroma (Danis, et al., 1955; Ellis, 1956), chronic iridocyclitis (Bürke, 1958; Cagianut, 1959; Senn, 1959), slowing and fractionation of the conjunctival circulation (Cagianut, 1958; Paufique and Royer, 1959).

Corneal signs are exceptional. Senn (1959) observed corneal ulcerations. Cagianut and Theiler (1959) noted, in a case of macroglobulinemia, a periodic-acid-Schiff-positive material between the corneal epithelium and Bowman's membrane.

In multiple myelomatosis (plasmocytoma) grayish or yellowish punctate or linear glistering crystals have been described, especially in the anterior portion of the corneal stroma (Meesmann, 1934; Markoff, 1948; von Sallmann, 1958; Bürki, 1958; Aronson and Shaw, 1959). These crystals are suggestive of cholesterol.

In other cases of paraproteinemia, crystals or punctate opacities of the cornea have also been noted: Palazón (1933); Blobner (1938); Palm (1947).

Oglesby (1961) described a corneal dystrophy in a patient with cryoglobulinemia and reticulohistiocytosis (lipoid dermatoarthritis). The corneal lesion appeared as an irregular geographic pattern composed of multiple polygonal gray opacities, which spared the limbal and central areas and which were located chiefly in the posterior fourth of the stroma, affecting also Descemet's membrane and the corneal endothelium.

These observations and the fact that it is only since Apitz's research work (1940) and the use of electrophoresis that the existence

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of a paraproteinemia could be properly diagnosed, lead us to suppose that corneal degeneration in this condition is, perhaps, not so rare as one might think.

Case report

This is a case of a man, aged 70 years, who has been complaining of diminution of vision for two years.

Antecedents. At the age of 29 years, the patient had pneumonia followed by purulent pleurisy which had to be drained. He also had a duodenal ulcer which gave rise to several hemorrhages and was operated upon in 1957; a blood transfusion was necessary.

His maternal grandmother was blind but the cause was unknown. Our patient has a son in good health but four other children were still-born and twins died two days after birth.

Ophthalmologic examination (November 4, 1959). There was a corneal dystrophy affecting the posterior layers of the cornea and accompanied by some epithelial alterations (fig. 1). These lesions principally affected the central region; the extreme periphery remained intact.

The other refractive media were normal. The fundus showed no alteration; the disc was neither atrophic nor excavated. There were no other anatomic abnormalities of the eyeball or adnexa.

Vision, after correction, was 1/20 in each eye.

The visual field (Goldmann's perimeter, tests 5/4 and 2/4) showed a very slight nasal narrowing without step on the left side. There was a complete field on the right side.

Ocular tension was a little too high, both on the right (25.8 mm. Hg) and on the left (23.8 mm. Hg). At the time of observation, the diurnal tensional curve oscillated between 29.4 and 31.7 mm. Hg on the right and between 29.4 and 34.5 mm. Hg on the left.

Scleral rigidity was low (O.D., 0.011 to 0.014; O.S., 0.007 to 0.014), which gave a higher corrected tension (up to 35 mm. Hg on the right and up to 41 mm. Hg on the left). Treatment with pilocarpine and Daramide reduced tension to normal (18.9 mm. Hg on both sides).

On February 27, 1960, a perforating corneal graft of six mm. was carried out on the right eye with eight edge-to-edge stitches. There were no operative incidents. During the following days, the wound showed no tendency to heal; in spite of an apparently perfect coaptation, the anterior chamber did not reform. At the end of a week, we were obliged to add another four stitches. The anterior chamber then reformed. There was no ocular reaction; the graft remained clear; the iris and the pupillary area were in perfect condition. We waited five weeks before removing the sutures; when we did, the anterior chamber was emptied; it was reformed during the following day. Torpid iritis then set in, without pain or ciliary injection; an anterior synechia formed and the pupillary area was gradually invaded by exudates, which finally gave rise to occlusion. The corneal graft remained transparent.

Histopathologic examination of the cornea (thickness 0.8 mm.) showed no significant changes

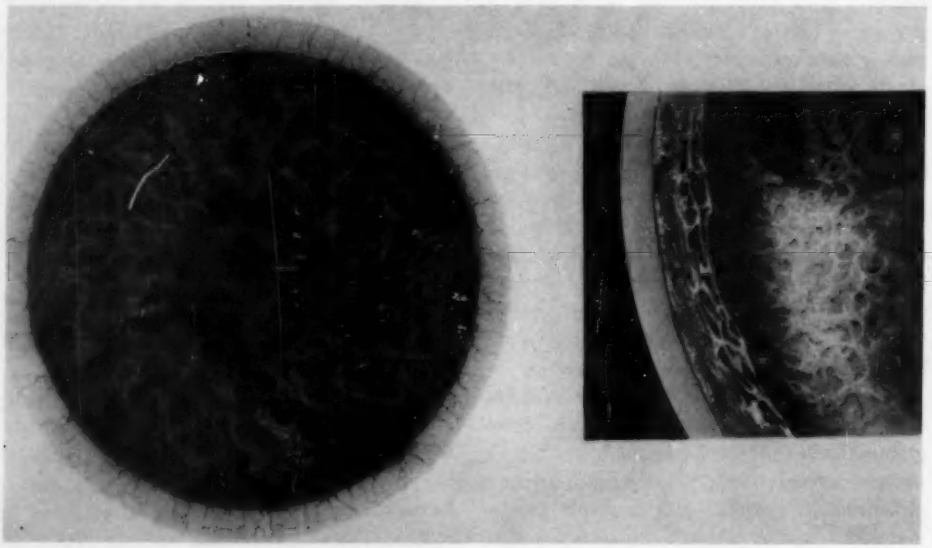

Fig. 1 (François and Rabaey). Corneal dystrophy.

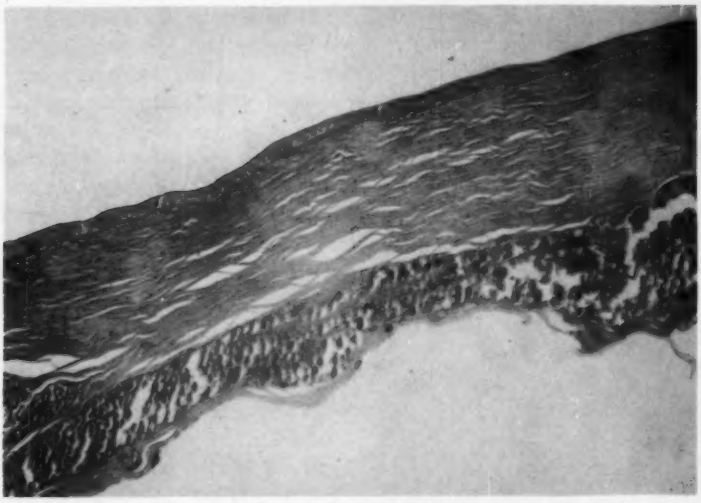

Fig. 2 (François and Rabaey). Cornea (×40). Trichromatic staining.

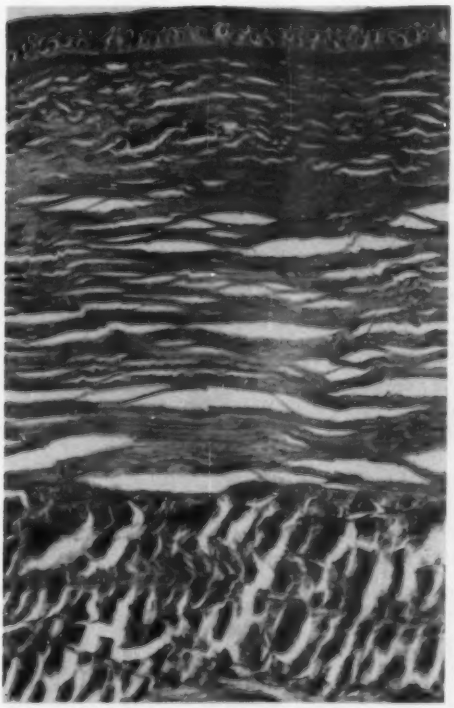

Fig. 3 (François and Rabaey). Cornea at higher magnification (×125). Trichromatic staining.

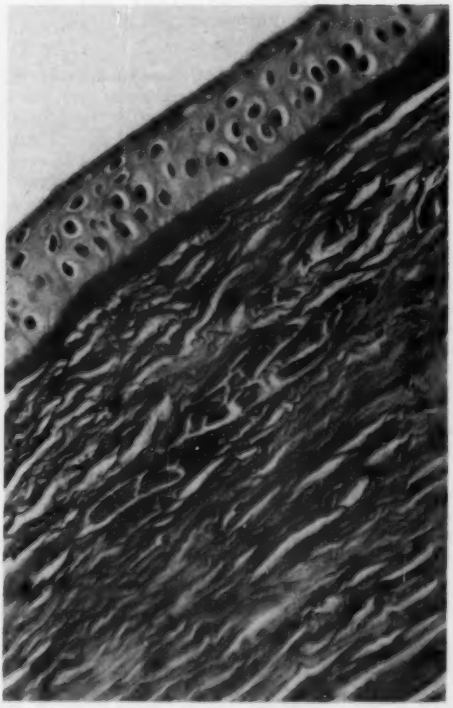

Fig. 4 (François and Rabaey). Anterior part of cornea (×250). Trichromatic staining.

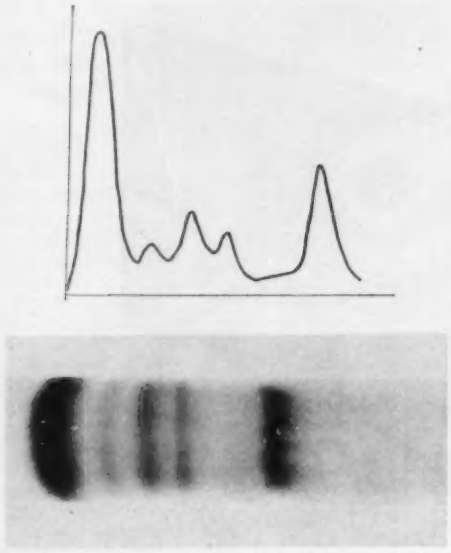

Fig. 5 (François and Rabaey). Paper electrophoresis of serum. Pherogram and diagram.

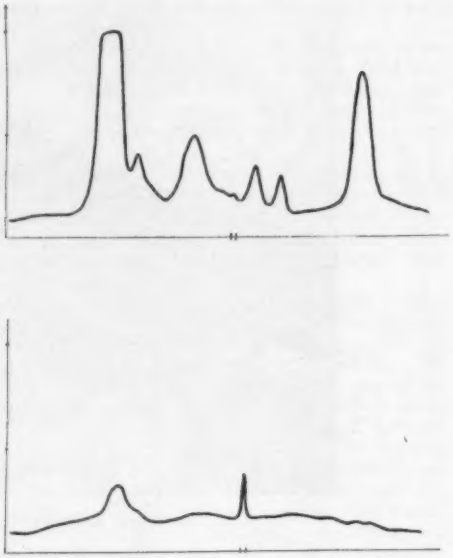

Fig. 6 (François and Rabaey). Agar microelectrophoresis (diagram) of serum and concentrated urine.

or real degenerative lesions of the epithelium. Here and there, however, the cells were larger than normal and of irregular arrangement. The superficial epithelial cells presented a normal positive PAS reaction. This staining also made it possible to recognize the basement membrane, which was everywhere intact. Bowman's membrane was also well observed.

The lesions really only affected the corneal substantia propria. At the level of the posterior third, there were no normal collagenous laminas; these had been replaced by a homogeneous and almost hyaline mass, more acidophilic than the corneal substance itself. After trichromatic staining this mass had a characteristic red color which contrasted with the blue of the collagenous bundles. Only in one part of the preparation were a few collagenous fibers seen traversing the homogeneous mass obliquely from front to back.

At the back the homogeneous mass was limited by a narrow area of better conserved parenchyma, but there also were small homogeneous masses here and there. Descemet's membrane was apparently normal, with more or less regular folds, following those of the narrow area of parenchyma.

The homogeneous, hyaline mass was not always of the same width or localization. Although affecting principally the posterior portion of the cornea, there were, nevertheless, in places several small, acidophil masses in the anterior layers of the substantia propria. They were easily recognizable by their red color after trichromatic staining.

After PAS staining the hyaline masses have the same pink color as the normal parenchyma. They do not show metachromatic staining with toluidine blue. With benzidine, followed by staining with Schiff reagent (protein reaction), they assumed a very definite red color.

The endothelium was almost completely absent, as is nearly always the case after corneal graft.

Discussion

The special clinical and histopathologic aspect of this cornea, which was unlike any other known corneal dystrophy, makes us

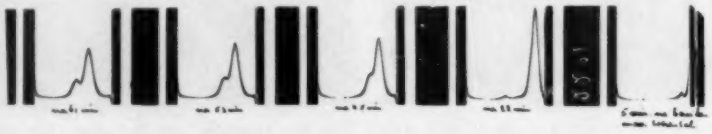

Fig 7 (François and Rabaey). Ultracentrifugation diagrams of the serum.

feel that the degeneration may have been caused by dysproteinemia. Electrophoresis of the serum confirmed this hypothesis.

Serum electrophoresis, on paper, showed, in fact, that normal γ-globulin was present in a very small quantity only. Where the median plane corresponding to a γ-globulin is usually found, there was an unusual fraction, important in quantity and with well marked limits (gradient M).

The total proteins of the serum were 6.3 percent and the proportions of the different fractions are given in Table 1.

After treatment of the pherogram with PAS reagent, the gradient M was only slightly stained.

After agar micro-electrophoresis the gradient M was very well marked. It migrated well in the agar and presented no striations, although there was a very slight undulation. The mobility of this fraction was very small; relative mobility in relation to serum albumin was 0.08. There were no other secondary gradients.

Sia test was negative. Agar micro-electrophoresis of urine, concentrated after ultrafiltration, gave an aspecific pherogram without gradient M.

After ultracentrifugation of the serum, no pathologic macroglobulin was found; the globulin count was slightly increased.

The sedimentation constants of the serum, diluted at one percent, are given in Table 2.

Systemic clinical examination was negative. Arterial tension was 150/90 mm. Hg. Radioscopy showed the arch of the aorta to be somewhat twisted and the heart inclined. The patient was very pale and nervous, slept badly and complained of headaches.

TABLE 1

PROPORTIONS OF PROTEIN FRACTIONS

	Percent of the Protein Fractions	Quantity of Each Protein Fraction in 100 ml. of Serum (gm.)
Albumin	49.5	3.12
α_1-globulin	6.8	0.42
α_2-globulin	12.2	0.77
β-globulin	8.3	0.52
γ-globulin	23.2	1.47

TABLE 2

SEDIMENTATION CONSTANTS OF SERUM

Components	Sedimentation Constant (S)
1. Physiologic Macroglobulin	16.1±0.9
2. Globulins	6.9±0.3
3. Albumin	3.6±0.2

Laboratory tests gave the following results: Sedimentation 43/75. Hematologic test: hemoglobin 87 percent, red cells 4,490,000 per mm.^{3}, white cells 6.100 per mm.^{3}; formula: eosinophils 5, basophils 1, neutrophils 48, lymphocytes 43, monocytes 3. Urea, 0.23 0/00. Thymol: 23.2 U. $ZnSO_4$: 20,3 U. Total cholesterol: 307 mg. 0/00, esterified 196 mgr. 0/00, ratio 64.5.

Radiography of the skull and the pelvis showed no abnormality. In the spinal column a degenerative disc lesion was seen between L4 and L5 with narrowing and compensative scoliosis; there was also a slight listhesis at L3. There was no decalcification of the skeleton.

The electrocardiogram is normal.

The myelogram after sternal puncture, showed the following results:

Myeloblasts	–
Neutrophilic promyelocytes	2
Eosinophilic myelocytes	1
Neutrophilic myelocytes	8
Neutrophilic metamyelocytes	–
Eosinophilic metamyelocytes	–
Neutrophils with rods	10
Eosinophils with rods	–
Segmented neutrophils	20
Segmented eosinophils	4
Basophils	–
Lymphocytes	12
Monocytes	–
Plasmocytes	*38*
(instead of 1 to 3)	
Histiocytes	5
Histioblasts	–
Megacaryocytes	–
Pronormoblasts	–
Basophilic normoblasts	3
Polychrome normoblasts	10
Acidophilic normoblasts	–
Histoid proliferation	–
Leuco-erythrogenetic ratio	8/1

Conclusion: multiple myeloma (plasmocytoma), medulla poor in cells.

This is a particular form of corneal dystrophy in a case of plasmocytoma without Bence-Jones albumin in urine.

This observation appears to us to be important for several reasons.

1. *A corneal dystrophy could be the first clinical sign of a paraproteinemia.* Therefore, in certain cases of atypical corneal degeneration, a systematic electrophoresis of blood serum should be made.

2. *A diagnosis of paraproteinemia,* in which the prognosis is generally bad, is less important from a therapeutic point of view, since there is no specific treatment, than from an operative point of view, when postoperative complications and on unfavorable evolution are to be feared, as in our case. It would be wise, it appears, to abstain from corneal grafting in such cases.

3. *It is recognized that plasmocytoma (myeloma)* and primary macroglobulinemia (Waldenström's disease) may be accompanied by such variable symptoms that diagnosis is often difficult. One sign, however, is constant: these two conditions are always characterized by the presence in the blood of a paraprotein, recognizable by electrophoresis (Regniers et al., 1957; Wieme, 1956).

It is certain, on the other hand, that paraproteinemia will not be found in any other kind of disease, except in rare cases of lymphatic leukemia or malignant lymphoma. It is also unlikely that a corneal dystrophy would develop only in a certain type of plasmocytoma or macroglobulinemia. In our case we found no pathologic macroglobulin after ultracentrifugation of the serum.

4. *It is important to know the nature of the substance accumulated in the cornea.* At the moment it is impossible to say if it is the serum paraprotein or some other substance.

There are, however, two reasons for thinking that the stored-up substance is not in liquid state in the cornea: (1) corneal puncture produced no liquid and (2) the sectioned surface of the substance was perfectly straight.

In certain cases of myeloma there is paraamyloid infiltration into the kidney and sometimes into other tissues. In these cases there is always a decided proteinuria which was not present in our case. Histopathologic examination of a small piece of skin showed no trace of any abnormal substance.

It is not impossible that macroglobulin might be deposited in a tissue with a slow flow, such as the cornea. In our case, however, it would appear more plausible to suppose that the accumulated substance is a derivative or some combination of the paraprotein, such as, for instance, a combination of strongly basic protein with the acid mucoid of the cornea.

It is possible that with this case similar manifestations might be found in the joint or ear cartilage. For this more research will be necessary.

Summary

A deep corneal dystrophy of a particular type due to a plasmocytoma is described, which was revealed by electrophoresis of the blood serum and by the myelogram.

De Pintelaan.

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CHRONIC PSEUDOTUMORAL EDEMA OF THE CONJUNCTIVA*

Of possible myxedematous and amyloid origin: With report of two cases

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The justification for presenting these two case histories (one of which was published in 1954[1] but which now requires re-evaluation) and for discussing their etiology in some detail is that a review of the available literature has revealed no cases in which pseudotumors of the conjunctiva have been considered from the standpoint of possible myxedema and amyloidosis.

Case reports

Case 1

A 34-year-old white woman was first seen October 26, 1954, complaining of occasional frontal headaches. Her previous history was not relevant. External examination of the eyes and ophthalmoscopic studies were negative and no errors of refraction were found. No treatment directed to the eyes was considered necessary.

On April 26, 1956, the patient returned complaining of redness and discomfort in the right eye for the previous week. Examination of the left eye was negative. On the right side there was some edema of the lower bulbar conjunctiva and some thickening of the plica semilunaris. The discomfort disappeared after a week of treatment with chloramphenicol and hydrocortisone drops every two hours, but the gross appearance of the right eye remained unchanged at this time and on subsequent visits in August, 1956, and February, 1957.

When the patient was next seen, April 13, 1959, she complained of a burning sensation in the right eye. There was now a slight ptosis of the right upper lid, which was two mm. lower than the left upper lid. The most striking lesion in this eye, however, was an apparent tumor mass in the lower bulbar conjunctiva (fig. 1-A), which extended from the lower fornix upward for six to eight mm., to a point three mm. from the limbus on the nasal aspect and six mm. from it on the temporal aspect.

The thickening noted for the first time in April, 1956, in the plica semilunaris was now considerably increased and was continuous with a light-pinkish, somewhat indurated area in the adjacent bulbar conjunctiva (fig. 1-B). The total lesion measured seven mm. in diameter and was 1.5 mm. high. The bulbar conjunctiva was edematous from the upper horn of the plica on the under aspect of the upper lid for an area extending eight or 10 mm. from the upper fornix to a point about five mm. from the limbus. This area, which extended to the outer canthus, was pinkish and was elevated about one mm. When pressure was applied, the lesion could be depressed, which showed that the edema was of the soft variety, but it returned to its original elevation when pressure was released.

* From the Department of Ophthalmology, University of Puerto Rico School of Medicine. Presented at the annual meeting of the American Ophthalmological Society, Colorado Springs, Colorado, May, 1960.

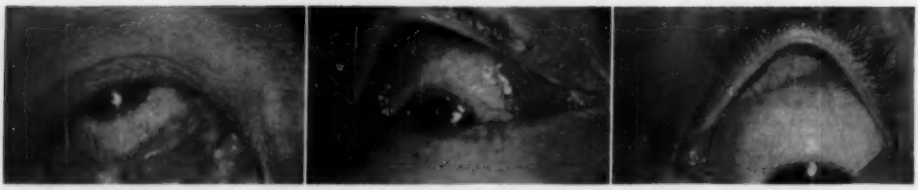

Fig. 1 (Picó). Conjunctival and other lesions in Case 1. (A) Lesion in lower bulbar conjunctiva of the right eye in May, 1959. (B) Infiltration of plica semilunaris and of nasal and upper bulbar conjunctiva of same eye in May, 1959. (C) Infiltration of upper bulbar conjunctiva of left eye in May, 1959.

The tumor mass in the lower bulbar conjunctiva was continuous with the inferior horn of the plica and with the mass in the nasal conjunctiva. It also extended to the external canthus, thus completing the ring formed by the thickened upper bulbar conjunctiva, the plica and the thickened nasal bulbar conjunctiva. The lesion did not extend to the limbus but encroachment upon it by the mass seemed imminent.

This lower lesion, which was elevated three or four mm., had a smooth surface but the contour was irregular because it consisted of three masses, which seemed superficially to be separate but which arose from a single wide base. They moved only slightly on pressure. The base was not pedunculated and was fairly well defined.

The triple lesion was light pink and was much more indurated than the affected area in the upper bulbar conjunctiva. This lesion and the lesion on the nasal aspect of the eye (that is, the hypertrophied plica and the adjacent involved bulbar conjunctiva) formed a fold over part of the more central normal bulbar conjunctiva. All the involved areas oozed slightly when scraped with a cotton swab. There was no evidence of discharge in the conjunctival sac.

The lesion in the lower bulbar conjunctiva had the appearance of being hard, but, although it was slightly indurated, it could be depressed with pressure, and it moved slightly with the rest of the bulbar conjunctiva.

The areas of bulbar conjunctiva nearer the limbus and not involved in the pathologic process described were normal except for slight injection. This area extended five mm. above the limbus, three to four mm. on the nasal side, three to six mm. below, and eight mm. toward the temporal side.

There were similar changes in the left side (fig. 1-C), but they were much less pronounced and apparently much earlier. In the upper bulbar conjunctiva a slightly elevated, soft, pinkish infiltration extended downward from the fornix for eight mm. There was also a slight engorgement of the plica, and there was an area of very slight edema, about one mm. wide in the lower fornix. Otherwise, the bulbar conjunctiva was normal on this side.

The palpebral conjunctiva was normal in both eyes. Ocular rotations and muscle balance were normal, as were the cornea, lens and eye grounds Measurements with the Hertel exophthalmometer were 12 mm. in both eyes. Tonometric measurements (Schiøtz) were 18 mm. Hg on both sides.

Laboratory examinations. Urinalysis, the Kahn serologic test, a complete blood study, and examination of the stools for parasites and ova revealed no abnormalities.

Smears of conjunctival secretion taken from both eyes showed only a few small groups of epithelial cells, all normal, and no leukocytes. Cultures of the secretions in blood agar and thioglycolate broth showed a growth of hemolytic Micrococcus pyogenes aureus in both eyes. Coagulase, gelatin and mannitol tests were negative.

Histologic studies. A specimen obtained May 15, 1959, from the middle of the large triple lesion in the lower bulbar conjunctiva was reported as follows:

The specimen consists of two elliptical portions of tissue measuring, respectively, six mm. and 1.4 cm. in diameter. The tissue is somewhat fibrillar and one aspect shows a grayish-white, glistening membrane.

All tissues were embedded. Histologic examination (hematoxylin and eosin) shows the conjunctival epithelial layer to be thinner than usual but otherwise not remarkable. The subjacent connective tissue shows fibroblasts widely separated from one another by pink deposits of a foreign material that is very finely granular and that is disposed in both fine and coarse strands. A few lymphocytes and very occasional plasma cells are observed. A few capillaries and a few moderately wide and empty endothelium-lined channels were also observed and were regarded as possible lymphatic capillaries.

Examination of tissues stained with hematoxylin and eosin showed pink deposits in the subconjunctival connective tissue, not solid and homogeneous but like a meshwork. There was no multiplication of fibroblasts and no inflammatory infiltration except for scattered lymphocytes. There were few nuclei. The conjunctival epithelium was thin but normal. With the crystal violet stain, the foreign material took on the purple color of amyloid but lacked the homogeneous appearance usual for that substance. The Congo red stain for amyloid was negative. The PAS (periodic acid Schiff) stain, which some but not all observers use as a test for amyloid, was light red and moderately positive.

With the Van Gieson stain the deposits appeared light greenish-yellow; no collagen was present. Several other stains were used but are not pertinent to the point at issue. The pathologist's conclusion was that while the result of the crystal violet stain was suggestive of amyloid, the nature of the deposit remained undetermined.

Follow-up. When the patient returned for examination in February, 1960, about a month after the uncomplicated birth of her third child in three and a half years, it was noted, for the first time, that apparent myxedematous changes were present, including dryness of the skin, partial loss of hair on the scalp, and loss of hair in the outer third of the eyebrows. She was at once referred to an endocrinologist, Dr Roberto Busó, for an endocrinologic study. The pertinent portions of his report follow:

The skin appears pale and dry, but it is not coarse, scaly or yellowish, even over the elbows. It is generally cool. The upper and lower eyelids reveal a moderate degree of nonpitting, baggy edema on both sides. The hair, which is dull and dry, is apparently thinning over the scalp and is definitely thinning over the lateral third of both eyebrows. The hair in the axillary and pubic regions appears normal. The nails are thin and brittle. The thyroid gland is not palpable. The remainder of the physical examination reveals nothing abnormal.

Laboratory tests, all within normal limits, included determinations of cholesterol; fasting blood sugar (Somogyi); nonprotein nitrogen; uric acid; urea nitrogen; total protein; and the albumin-globulin ratio. Electrophoretic preparation of proteins revealed a normal fractional globulin distribution (alpha 1.5 percent; alpha 2.8 percent; beta, 20 percent; gamma, 22 percent).

The basal metabolic rate was reported as —25. The I^{131} uptake was 9.2 percent in 24 hours. Roentgenologic examination of the chest and the orbits revealed no abnormalities.

Dr. Busó's conclusions were as follows:

A clinical review by systems permits a diagnosis of structural changes in the skin and appendages compatible with the diagnosis of hypothyroidism, though no system other than the ocular appears involved at this time. The ocular manifestations could very well be the earliest manifestation of so-called localized myxedema, preceding the skin manifestations by a period of several years. In this case, secondary hypothyroidism can be ruled out. There is no history of head trauma; menstrual absence; difficulties during labor; postpartal hemorrhage; structural and functional changes in the breast with absence of lactation and atrophy of the vaginal mucosa; or loss of pubic and axillary hair. The presumption of primary hypothyroidism is further supported by the I^{131} uptake in 24 hours, which is less than 10 percent, as it usually is in primary myxedema, though not in secondary myxedema. The importance of the etiologic classification of primary hypothyroidism appears immediately in this particular case, because primary hypothyroidism is usually associated with an increased amount of circulating thyrotropin, which has been shown experimentally to produce infiltrative ophthalmopathy.

The patient was started on thyroid (60 mg. daily) March 10, 1960. The use of thyroid extract in infiltrative ophthalmopathy is based on the premise that an increase in the amount of thyroxin in the circulating blood will decrease the amount of circulating thyrotropin and thus decrease its possible effect on the eyes.

In view of the developments in this case, the biopsied specimen was transmitted to the Armed Forces Institute of Pathology (AFIP Accession No. 953167) for further examination. The substance of the report, by Dr. Lorenz E. Zimmerman, is as follows (fig. 2):

"Sections prepared from the paraffin block reveal the substantia propria to be markedly thickened by amorphous, relatively acellular masses of hyalin material which both morphologically and tinctorially appears to be amyloid. In many places the accumulated subepithelial material has caused an irregular nodularity of the surface. The epithelium frequently is thinned out over the underlying mounds of amyloid. Between adjacent mounds there are usually tubules of surface epithelium containing large numbers of mucinous goblet cells. The cells contained within the amyloid deposit are often unidentifiable mononuclear elements, but a moderate number of macrophages, plasma cells, lymphocytes and polymorphonuclear leukocytes can be identified. No one cell type appears to predominate.

"The stromal deposits exhibit a variable eosinophilia, in places staining a faint pink while in other areas there are varying shades of rose to red. With crystal violet this material exhibits the typical metachromatic staining reaction of amyloid, but the resultant shades vary greatly from pink to magenta to violet. With the periodic-acid-Schiff reaction, there is only an extremely faint positivity. The alcian blue and colloidal iron methods for acid mucopolysaccharide give essentially negative staining reactions. With the Masson trichrome stain, the deposits generally stain a faint greyish-blue to bluish-purple.

"This is an unusually fine example of conjunctival amyloidosis."

Case 2

A summary of the case of chronic pseudotumoral edema of the conjunctiva reported in 1954 is as follows:

This white woman, now 38 years of age, was first seen in December, 1951, with the complaint of a fleshy growth in the right eye. It had increased in size over the year it had been present, and it was associated with itching and a slight discharge in both eyes, worse in the affected eye. The previous history was otherwise irrelevant, and general physical examination revealed nothing abnormal.

External examination of the right eye showed a hard, hypertrophied, congested plica semilunaris, which could be palpated through the upper eyelid

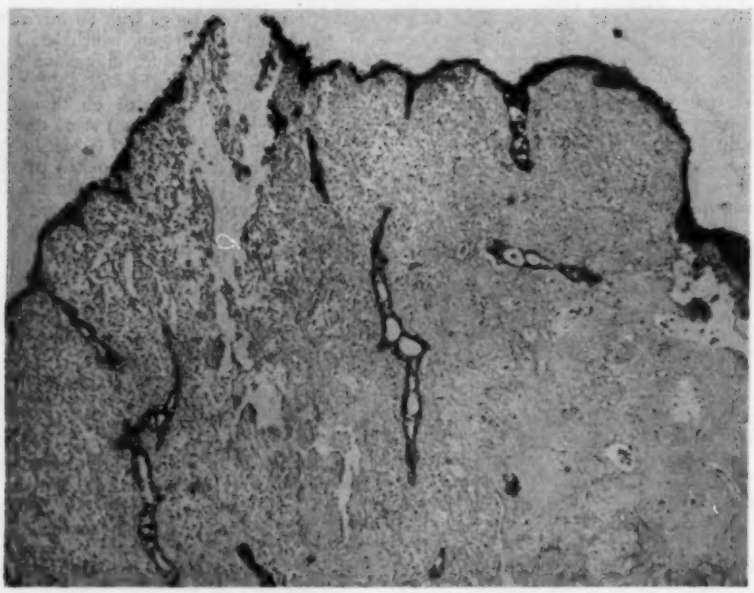

Fig. 2 (Picó). Photomicrograph of excised specimen in Case 1. Note the amorphous, relatively acellular masses of hyalin material in the substantia propria (×35).

when the eye was closed. A small pterygium, which had invaded the cornea for one mm., presented in the nasal side of the right eye. The plica semilunaris on the left side was slightly reddened but not hard. Both eyes showed a slight congestion of the palpebral conjunctiva.

Routine laboratory examinations, including the Kahn test, were negative. Smears and culture of the conjunctival secretion in both eyes were also negative.

The tentative diagnosis was possible new growth of the right plica semilunaris. No improvement followed the use of chloramphenicol drops and ointment, and multivitamins and antihistamine therapy by mouth, for two weeks. Cortisone drops were also ineffective.

In January, 1952, a biopsied specimen from the upper horn of the right plica semilunaris was reported to show fibrosis and edema of undetermined origin. The pathologist reported as follows:

"Most of the specimen is composed of fibrous tissue that is moderately well vascularized. The tissue is dense and collagenous peripherally but appears edematous in most of the central portions. The edema extends to the walls of the small blood vessels. One side of the specimen is covered by conjunctiva that is lightly broadened in some areas and is atrophic in others.

"A Van Gieson stain shows the collagen fibers at the periphery very well. The central portions of the specimen stain green and contain relatively few red fibrils. In spite of the color reaction, it is believed that the green areas probably represent simple edema and not an amyloid infiltration. Special stains for amyloid could not be used because the small size of the specimen required its total embedding in paraffin."

About two months later (March 1952), some hardening and hypertrophic changes were first noticed in the left plica semilunaris, but these changes were much less marked than in the right eye.

For the next 10 months, the condition of both eyes remained substantially unchanged. Then it was first noticed that, while the plica semilunaris remained unchanged, there was some thickening as well as some congestion of the bulbar conjunctiva under the right upper eyelid, extending from the upper fornix downward for about eight to 10 mm. The process appeared, as in the case just reported, to be a prolongation of the upper horn of the plica upward and temporally almost to the external canthus. A similar hypertrophy was observed in the upper bulbar conjunctiva on the left side, but the change was less pronounced than on the right.

The thickening of the plica semilunaris and the upper conjunctiva in both eyes remained about the same for the next years, but in April, 1957, it was necessary to remove the pterygium in the right eye, which had invaded the cornea for two mm. The results were excellent. The excised tissue appeared to be an ordinary pterygium and it was not examined in the laboratory.

In July, 1959, when the patient was next seen, the status of the right eye was unchanged, but the thickening of the plica semilunaris and of the upper bulbar conjunctiva on the left side was somewhat more marked.

Follow-up. In view of the developments in the

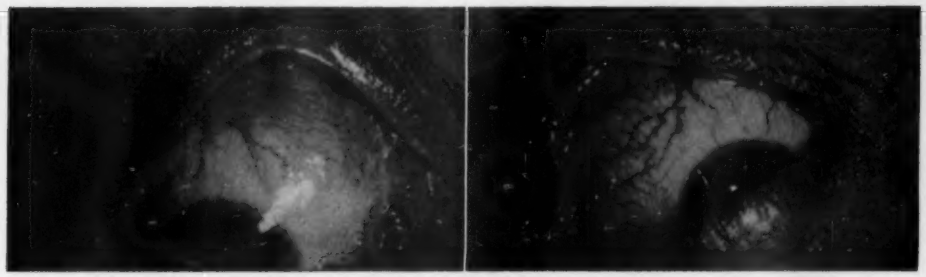

Fig. 3 (Picó). Conjunctival and other lesions in Case 2. (A) Infiltration of upper bulbar conjunctiva and plica semilunaris of right eye in March, 1960. The upper horn of the plica was included in the biopsy performed in January, 1952. (B) Nodule in tarsal conjunctiva of upper eyelid, hypertrophy of plica semilunaris, and infiltration of upper bulbar conjunctiva of left eye in March, 1960.

apparently similar case just described, this patient was asked to return for further observation and studies. When she was examined March 11, 1960, the hypertrophy of the right plica semilunaris had not advanced but the thickening of the upper bulbar conjunctiva was more pronounced; the involved area was about two mm. thick and extended downward from the fornix for eight mm. (fig. 3-A).

The changes in the left eye were much more remarkable (fig. 3-B). The thickening of the plica semilunaris was now comparable to that observed on the right side when the patient was first seen in December, 1951. When the left eye was closed, a pea-sized mass could be palpated through the upper lid in the nasal third of the eye. When the upper lid was everted, the mass was found to be located at the level of the upper border of the tarsus, in the transitional conjunctiva, and to be continuous with the upper horn of the thickened plica semilunaris and the thickened upper bulbar conjunctiva. It was waxy-yellow, irregular, and indurated, and it measured about eight mm. horizontally, five mm. vertically, and five mm. in thickness.

As on all previous examinations, the lens, vitreous and eyegrounds were bilaterally negative. Biomicroscopy showed small, diffuse pigment deposits on the corneal endothelium in both eyes, especially the left. Ocular rotation and muscle balance were normal. Vision was 20/20 in each eye. Measurements with the Hertel exophthalmometer were 16.5 mm. on the right side and 16 mm. on the left. Tonometry (Schiøtz) showed pressure of 19 mm. Hg in the right eye and 13 mm. Hg in the left.

When the patient was questioned on this visit, she stated that for the past two years she had been aware of some loss of hair, especially over the scalp, and of easy fatigue. In July, 1959, her family physician had referred her for an endocrine study. The 24-hour I^{131} uptake was 15 percent. He did not consider thyroid medication.

She was referred to Dr. Busó for an endocrine study which was reported as follows: "The skin is dry and finely scaly. There is some nonpitting infiltration over the dorsum of both hands and both lower palpebral regions. The hair is dull, dry, and scanty over most of the scalp and over the lateral third of both eyebrows. It is possibly decreased in both axillary regions.

"No abnormalities were found on urinalysis; complete blood study; blood cholesterol determination; total protein determination and electrophoretic partition of the serum albumin and globulin fractions.

"The basal metabolic rate was —12 and the radioactive iodine uptake in 24 hours was 13.7 percent."

March 18, 1960, a biopsy was taken from the left eye, including the upper two thirds of the plica semilunaris and the nodule in the tarsal and transitional conjunctiva of the upper eyelid continuous with the upper horn of the plica. A smaller specimen was obtained from the thickened bulbar conjunctiva near the fornix. The biopsied specimens were sent to the Armed Forces Institute of Pathology (AFIP Accession No. 953166) for examination. The substance of the report, by Dr. Lorenz E. Zimmerman, is as follows (fig. 4):

"Sections prepared from the two pieces of tissue reveal extensive stromal deposits of a fairly homogeneous hyalin substance which morphologically and tinctorially is consistent with amyloid. The conjunctival epithelium is extremely atrophic and largely reduced to a single layer of flattened cells. In many places, small tubular inclusions of conjunctiva are trapped deep in the stroma within the stromal deposits.

"While the lesions and amyloid deposits in this case are similar to those found in the other case of conjunctival amyloidosis (AFIP Accession No. 953167), there are some differences. With crystal violet, the metachromasia in the present case is somewhat less striking and less uniform than that observed in the other case. With alcian blue and with the colloidal iron technique for acid mucopolysaccharides the lesions of the present case do include areas where there is a fairly intense positive staining reaction while in the other case these stains were completely negative. The positive staining for acid mucopolysaccharides in the present case appears to be in the immediate vicinity of mesenchymal cells contained within the amyloid deposits. The bulk of the deposits, however, give a negative staining re-

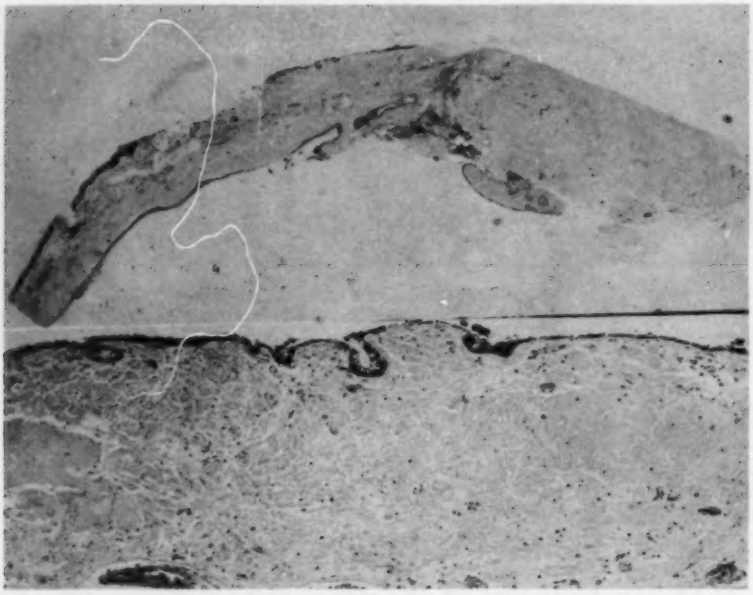

Fig. 4 (Picó). Photomicrograph of excised specimens in Case 2. Note stromal deposits of a fairly homogeneous hyalin substance (×5 and ×9).

action. The PAS positivity in the present case is more intense than in the other case."

In his report, Dr. Busó stated that the resemblance between this patient and the patient in Case 1 was apparent at first glance. Particularly striking was the chronologic sequence of localized conjunctival infiltrates for a number of years before clinical manifestations in the skin and appendages led to an investigation for possible hypothyroidism. The evidence from the laboratory was not as striking as in the previous case, but the data were not sufficient to overturn the clinical evidence. The response to thyroid medication, upon which the patient was started, will settle the question.

At the time this patient was first observed, it was speculated that the change in the semilunar fold might be a very uncommon sequel of a mild chronic conjunctivitis, which perhaps had induced a proliferation of fibrous tissue in the plica and a local circulatory embarrassment manifested as edema. Now, there seems little doubt that, as in the first case, the correct diagnosis is hypothyroidism and amyloidosis.

Amyloidosis

The course of events and the findings in both of these cases require the discussion of two processes, amyloidosis and myxedema. The following statements on amyloidosis are taken chiefly from Duke-Elder's[2] excellent description.

Amyloidosis is a relatively uncommon condition, characterized by the deposition in the tissues of a substance which has a metachromatic staining property. Amyloid, which is a variety of hyaline substance, is given a special name because of its more or less constant affinity for several unrelated stains, which characteristically stain it a different color from that of the stain used. The name was originally employed because amyloid stains somewhat like starch with iodine. The staining reactions are sometimes doubtful (the paramyloid reactions of the European medical literature). My own, entirely speculative, opinion is that the negative results with some stains ordinarily used for amyloid may be explained by the fact that the myxedematous infiltrate which eventually produces amyloid material has not yet been transformed into amyloid at the time the study is made. It is well known that in primary amyloidosis, which both of the reported cases represent, the amyloid material often stains atypically, while in secondary amyloidosis the staining reactions are typical.

Microscopically, amyloid appears as an acidophilic, homogeneous material which is deposited extracellularly in various tissues. While its origin and chemical composition are not yet entirely clear, Hass and his group,[2-5] in their investigation of secondary amyloidosis, found that there are at least two protein fractions in the liver of humans dying of chronic pulmonary tuberculosis, as well as a polysaccharide of the chondroitin-sulfuric acid type. The polysaccharide is present in variable amounts and comprises up to 1.5 percent of the amyloid. Rukavina and his associates,[6] in 1956, found abnormal lipoprotein fractions and an abnormal type of A_2-globulin in one family with primary amyloidosis.

Though the factors which govern its formation and deposition are not yet clear, amyloid is generally considered to be the result of a disturbance of protein synthesis in the tissues. It is postulated that it is the end-result of an antigen-antibody reaction, but the theory is based on experimental data only. Hass and his associates argue that a most positive piece of evidence against the fundamental importance of antigenic stimulation in the genesis of amyloid disease is the frequent absence of the disease in prolonged and intensive stimulation of immune mechanisms. Heredity is apparently a factor in some cases. Falls and his group,[7] in 1955, reported that they had found 154 cases of hereditary primary systemic amyloidosis in the literature.

There are four types of amyloidosis: (1) primary; (2) secondary, which is the most frequent; (3) local amyloid tumors; and (4) amyloidosis with multiple myeloma. The localized variety, which the two cases reported in this communication apparently represent, is characterized by the formation of small solitary or multiple tumors in the eye, bladder, urethra, pharynx and larynx.

The clinical manifestations of amyloidosis depend upon the type of disease, the extent of the condition, and the kinds of organs involved. They may simulate the clinical picture of many other diseases.

The eye and its adnexa may be extensively involved in both primary and secondary disease, but amyloidosis of the conjunctiva, according to Duke-Elder, is only very occasionally a part of a general disease process. On the contrary, it is almost invariably a local disease. As such, it may appear in three forms: (1) as an incidental degenerative process in such pathologic conditions as old trachoma scars; (2) as a clinical entity sui generis; and (3) as a plasmoma or hyalinoma.

Amyloidosis of the eye, appearing as a separate disease as in these two cases, was first described in 1871 by von Oettingen of Dorpat. It was subsequently studied by Raehlmann, Kubli, Vossius, Kamocki, and Rumschewitsch between that date and 1892. In 1930, Katayama, in a review of the literature, collected 110 cases in the European literature after von Oettingen's original observations, and 23 additional cases in the Japanese literature. It is possible, of course, that many instances of amyloid disease supposedly arising in trachomatous scars may really be primary and bear little actual relation to the original infection.

Ocular amyloidosis most often attacks young adults, especially those between 25 and 30 years of age. It affects one eye or both eyes; about two thirds of all cases are bilateral. The degeneration is local and the cause is obscure, for the patients are almost invariably healthy and show no signs of general amyloid disease. The two cases reported conform in all respects to these criteria.

Amyloid disease in the conjunctiva usually begins in the transition fold and extends from this point to the tarsal and bulbar conjunctiva. The mucous membrane appears yellow, waxy, transparent and avascular. The tumefaction may be of considerable size. As tarsal involvement proceeds, the tumors on the upper lids may be of such size that the patient can scarcely open his eyes. In some cases, the entire conjunctiva and semilunar fold present irregular masses so brittle that they are readily torn, with, however, very little bleeding, when the lids are forcibly opened. The cornea may be involved

in the degenerative process, either in toto or in a band-shaped area. More often, the cornea is disorganized by pannus.

The disease progresses slowly but inexorably, and medical treatment is peculiarly ineffective. According to Duke-Elder, surgery is the only possible course when the masses, by their size and weight, prevent opening of the eyes. If extensive excision is necessary, a graft from the mucosa of the lip must be employed to compensate for the defect; the conjunctiva is too friable to serve for this purpose. Complete removal of the mass is usually neither possible nor advisable. Fortunately, the portion left in situ tends to shrink spontaneously, although in some instances gross recurrence has been observed. In the second of my cases, the second biopsy served, in effect, as a removal of the mass in the upper lid. In the first case, surgery may be necessary if there is no improvement on thyroid medication.

The appearance of the lesions in my own cases is similar to the appearance of other cases reported in the literature as amyloidosis of the conjunctiva, by Elles[8] and Coats,[9] among others. The case of "solid edema" of the conjunctiva reported by Coats in 1915 is strikingly similar. In this case, the whole eyeball was eventually surrounded by nodular, indurated masses, and exophthalmos developed. Although the masses were also retrobulbar, the final diagnosis was amyloid disease of the conjunctiva.

Coats' case, like my own, illustrates the fact that stains for amyloid tissue are not uniformly positive. He wrote:

> Anteriorly practically all the degenerated bundles and masses give the characteristic coloration in a typical manner. Posteriorly, on the other hand, many bundles show pronounced homogeneous changes without the distinctive staining reaction, others show it in an incomplete or not wholly typical form, and the reaction is quite unequivocal only in the most degenerated areas and in the larger masses of homogeneous substance. It seems evident, therefore, that the swelling and loss of structure in the least affected bundles represents a preparatory or preliminary stage towards the formation of true amyloid substance.

It is significant, as this description seems to suggest, that edema of some sort, which does not give the proper staining reactions for amyloid, is present early in the pathogenic process of amyloidosis. Certain other reports in the literature, Slavík's[10] among them, point to the same discrepancy and confusion.

Combined amyloid-myxedematous disease

It may be that the explanation just advanced underlies the inconsistency of the results of the various staining reactions for amyloidosis in my own two cases. As in Coats' case, the explanation may be that the reaction varied in different parts of the specimen. The results of the first study raised the doubt that amyloidosis was the correct diagnosis, and the suspicion seemed warranted when both patients, years after their ocular manifestations first appeared, presented partial loss of hair, dryness of the skin, and other manifestations of myxedema. In both cases the diagnosis of primary hypothyroidism was confirmed by study by a competent endocrinologist and by the additional laboratory findings.

The question naturally arises as to the possible relation between myxedematous infiltration and amyloidosis of the conjunctiva. Coats mentioned that in his case there was "stationary enlargement of the thyroid *without symptoms* (italics mine) of Basedow's disease, cretinism or myxedema." The observation seems significant. One wonders whether, in view of the thyroid enlargement described, his patient might not have had goiter with myxedema, without general symptoms, and whether the diagnosis of malignant exophthalmos, of which I shall speak later, might not explain the subsequent clinical findings. Certainly the recent findings in both of my own cases suggest that the changes in the conjunctiva were the result of myxedematous infiltration, which may be a preliminary stage in the development of the substance that produces typical amyloid reactions. To express it in another way, the so-called amyloid product may be the result

of myxedematous infiltration that, changing in concentration and chemical composition, acquires, as a final stage, the staining properties that identify it as amyloid.

It is well known that edema of the conjunctiva, varying from mere pallor to, occasionally, definite edema, with protrusion of the conjunctiva between the lids, may be found in some cases of myxedema. A review of the available literature, however, has shown no cases in which the conjunctival edema was accompanied, as in my cases, by solid changes suggestive of tumor formation.

It is also well known that malignant exophthalmos occurs rather frequently after thyroidectomy for thyrotoxicosis, and that hypothyroidism is frequently another postoperative development. Thyroid medication is usually unable to halt the ocular process, and it may be that there are two possible explanations:

1. Thyroid medication may be unable to control the edema-producing action of the thyrotropic hormone.

2. Retrobulbar edema, increased by the infiltrate of myxedema that may appear after thyroidectomy, may have changed in histochemical composition to a material such as amyloid and for that reason does not respond to the edema-clearing properties of thyroid medication. Day[11] cites the observations of Wegelius and his associates which show that mucopolysaccharides with marked hydrophilic properties are increased in the orbital tissues in malignant exophthalmos. Day himself considers chemosis of the conjunctiva an obvious manifestation of this change.

Symmers[12] has called attention to the clinical and experimental studies of Pĕrasalo and Latvalahti on the relation between amyloidosis and endocrine secretions. These observers found that corticotropin, and, to a lesser extent, cortisone, encourages the development of experimental amyloidosis but that desoxycorticosterone had no such effect. Similarly, castration increased amyloid production, while testosterone had no such effect. Finally, thyroidectomy encouraged amyloidosis, while thyroid extract had an inhibitory effect upon the development. Symmers also mentioned the work of Uotila, Pĕrasalo and Vapaavuori, which showed that thyrotropin accelerates experimental amyloid formation and that the growth hormone does not have this effect.

Localized myxedema

The association of amyloidosis with malignant exophthalmos and localized pretibial myxedema in one of the cases described by Symmers requires some discussion of that association. A similar association was reported in 1949 by Curtis, Cawley and Johnwick,[13] who suggested that both the exophthalmos and the myxedema might be caused by a local effect of the thyrotropic hormone on the extraocular tissues and on the skin of the lower leg.

It has been shown that in both primary and secondary generalized myxedema, the thickening of the skin is not a true edema but is caused by the extracellular deposition of metachromatically staining mucinous material in the dermis. According to Gabrilove and Ludwig,[14] this material, which has not yet been defined chemically, is a complex of acid mucopolysaccharides and protein. The infiltrate observed in their cases disappeared when the patients were given 120 to 180 mg. of desiccated thyroid daily for six to eight weeks. These observers also found that in secondary (pituitary) myxedema, administration of the tropic fraction of the adenohypophysis (TSH) was as effective as the use of desiccated thyroid in causing the disappearance of the metachromatic substances in the skin, though it had no effect at all in patients with primary thyroid myxedema.

Gabrilove and Ludwig consider that it is no longer tenable to assume that the increased amount of mucopolysaccharides in the connective tissue of the skin is the result of the action of elevated levels of thyroid-stimulating hormone (TSH) or of the direct action of an associated pituitary fraction upon the

connective tissue. They believe that this point of view is negated by their investigation of identical changes in the skin of patients with pituitary deficiency, in whom circulating levels of TSH must be extremely low or entirely deficient. In their opinion, the factor that initiates the myxedematous process is most likely to be a deficiency of thyroid hormone (or its tissue-active form) at the periphery.

Certain other studies of pretibial myxedema are of interest in this connection. Watson and Pearce[15] found the extracellular material present in these lesions to be composed of the acid polysaccharides chondroitin-sulfuric acid and hyaluronic acid combined with protein in some form. They have advanced a local disturbance of mucopolysaccharides metabolism as an explanation of the pathogenesis of pretibial myxedema.

Beierwaltes[16] found that a deposit histologically similar to that in generalized myxedema was occasionally found locally in the pretibial skin of patients with thyrotoxicosis and malignant exophthalmos. When patients with localized pretibial myxedema were given 180 mg. of desiccated thyroid daily for periods up to eight years, no clinical or histochemical change occurred in the myxedematous plaques. In Beierwaltes' cases pretibial myxedema was observed in association with both hypothyroidism and hyperthyroidism. In a patient treated by X-ray therapy over the pituitary region, exophthalmos diminished, conjunctival edema and extraocular muscle palsy disappeared, and pretibial edema cleared completely in one leg and 80 percent in the other. McCullough, Ruedemann and Gardner[17] also found that localized myxedema present in a patient with exophthalmos disappeared completely with the onset of pituitary deficiency after surgery.

Beierwaltes, working with Bollet,[18] found that the acid mucopolysaccharide content of the skin in myxedematous pretibial areas of euthyroid patients who also had exophthalmos was considerably elevated as compared to the content of clinically uninvolved areas of the body. The uninvolved areas, however, showed a moderately increased concentration of acid mucopolysaccharides as compared with the concentration in skin taken from normal patients without thyroid disease.

Ludwig, Boas and Soffer,[19] in a study of the role of mucopolysaccharides in the pathogenesis of experimental exophthalmos in guinea pigs, found that the proptosis was caused by the accumulation of large quantities of intercellular ground substance and water in the orbital connective tissue. This was shown by the presence of large amounts of metachromatic material, of which hyaluronic acid was an important component, and by increase in the hexosamine and water content of these tissues. To these observers, these findings indicated that the pathologic changes in experimental exophthalmos are similar to those of localized myxedema in man and that a common mechanism probably accounts for both conditions.

In my own cases, as already pointed out, the findings suggest that the changes in the conjunctiva may be the result of localized myxedematous infiltration. To date, unfortunately, we have, in our hospital in Puerto Rico, no personnel with experience in technique of chemical assay of acid mucopolysaccharides and therefore we have not been able to measure the concentration of these substances in tissues removed for examination. The references cited, however, leave no doubt that both amyloid and the infiltrate of myxedema contain mucopolysaccharides, though the difference in concentration has not yet been determined.

Exophthalmos

It must be remembered that exophthalmos can quite as well be produced by the changes in the orbital tissues present in myxedema as by those present in thyrotoxicosis. This was shown by exophthalmometric measurements in 21 of the 34 patients with spontaneous myxedema reported by Galli-

Mainini.[20] There are two possible explanations. The first is that exophthalmos is the result of the unchecked water-storing action of the thyrotropic hormone, produced by thyroxin deficiency. The other explanation is that exophthalmos is the result of the infiltrate found in the skin and connective tissue in myxedema. Galli-Mainini considered that the explanation of exophthalmos in spontaneous myxedema was quite possibly the same as the explanation for it in thyrotoxicosis, that such patients retain water unduly and also have weak muscles. The exophthalmos produced in myxedematous animals by injection of thyrotropic hormone is probably on the same basis, in his opinion, that this hormone, through its water-storing action, aggravates the edema already present.

In another study of 200 patients with thyrotoxicosis, with variable states of thyroid dysfunction, Day[11] found that the exophthalmometric readings in 26 patients with chemosis of the conjunctiva varied from 13.5 to 29.5 mm. and averaged 22.4 mm.

These various observations suggest the possibility that chemosis of the conjunctiva may exist without proptosis when there is little or no edema of the orbital tissues and that the degree of proptosis inceases as edema of the orbital tissues increases.

Unreported studies on myxedema and amyloidosis

After I had concluded, from my own cases and a review of the literature, that it is quite possible that the amyloid substance found in the conjunctiva in these cases was probably preceded by a localized myxedematous infiltration in that area, similar to localized pretibial myxedema, I found apparent corroboration of my conclusions in unpublished experimental work by Dr. Carmen B. Casas, of the Department of Physiology of the University of Puerto Rico School of Medicine.[21] Working with inbred mice chronically treated with thiourea, thiouracil and propylthiouracil, she found a high incidence (more than 80 percent) of generalized amyloidosis in both sexes, whether or not the gonads were in situ. She also found evidence of colloid goiter, which shows that the thyroid was inhibited by the chronic therapy. When the thyroid gland was totally destroyed by radioactive I^{131}, the animals that outlived the radiation by 12 months or more consistently showed generalized amyloidosis.

Conclusions

There are certain striking similarities between amyloidosis and myxedema, as these various reports show. To sum them up:

1. The amyloid material deposited in amyloidosis and the myxedematous infiltrate found in the skin in generalized myxedema, in pretibial myxedema, and in the orbital tissue in malignant exophthalmos all show metachromatic staining properties.

2. The chemical composition of this material has always been shown to be a protein or a protein combined with polysaccharides.

3. The presence of thyroid disease, or a history of former thyroid disease, in many reported cases of amyloidosis is striking. In all instances, however, the thyroid disease was apparently considered an incidental, unrelated finding, probably because it was thought to be due to the deposition of amyloid in the thyroid and not to primary thyroid disease of the type that could produce a myxedematous state.

4. Ocular involvement is not uncommon in amyloid disease. In a study of ocular findings in hereditary primary systemic amyloidosis, Falls and his associates[7] found retinal periarteritis, with or without dense hyaline vitreous opacities, to be an important manifestation. Exophthalmos was frequently present in these cases, but the basal metabolic rates and radioiodine uptake studies were not reported. Of the six patients in this group, one had a thyroid enlargement and another malignant exophthalmos which progressed after thyroidectomy. In 1959, Kaufman[22] reported primary familial sys-

temic amyloidosis in three members of the same family, one of whom had a small thyroid nodule. It thus seems possible that the basis of so-called familial or hereditary primary systemic amyloidosis is a hereditary insufficiency of the thyroid or an insufficient utilization of thyroxin by the tissues. It is well established that thyroid deficiency can be inherited.

5. Experience has shown that malignant exophthalmos is seldom reversible with thyroid therapy. The same holds for most instances of pretibial edema that occur in association with exophthalmos. The explanation is probably the presence of amyloid, which has been postulated as the final chemical change in the myxedematous infiltrate. In my own cases, my theory is that the lesions in the conjunctiva have advanced from localized myxedematous infiltration to amyloidosis. They may not regress under the thyroid therapy that has been instituted, but the method is worth a trial; it may arrest further development of the lesions now present and may prevent the appearance of new lesions.

As has been evident from the line this presentation has taken, my own theory is that all types of amyloidosis may be secondary to a state of hypothyroidism, with so-called primary amyloidosis really not primary but secondary to myxedema. In tuberculosis and other chronic diseases and infections, as well as in multiple myeloma, there may be an excessive demand for thyroxin by the general metabolic processes, and this demand may create a hypothyroid state in some tissues, the localized hypothyroid state leading to localized myxedematous infiltration. The myxedematous infiltrates, then, may in time become converted into amyloid. The observations in the cases reported in this communication, numerous reports in the literature, and Casas' unpublished experimental studies[21] all lend support to this hypothesis.

This theory is, of course, at present no more than a theory. Numerous questions arise that must be settled in the laboratory. Is amyloid a substance that develops from myxedematous infiltrate? Do the infiltrates in the orbit and in the skin in pretibial myxedema produce the characteristic staining reactions of amyloid? Is the amyloid postulated as a development from myxedematous infiltrate a different substance but still a substance that depends for the formation on the abnormal local metabolism in the tissue that results from a deficiency of thyroxin?

Related to the theory just advanced is the further theory that malignant exophthalmos and pretibial localized myxedema may also have the same pathogenesis. That is, they are probably the result of amyloid deposits resulting from myxedematous infiltration in the pretibial area and in the orbit.

The multiple loopholes in the hypothesis just presented are fully realized. It is hoped, however, that enough interest has been aroused in the possible cause and effect relation between hypothyroidism and amyloidosis to put ophthalmologists, endocrinologists, pathologists, biochemists, and others to work on the problem.

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THE MUSHROOM GRAFT*

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The use of a combined lamellar and perforating corneal graft was first described by Franceschetti and Doret in 1950. Because of its suggestive shape they called it a mushroom graft. They felt that it combined the trophic and other advantages of lamellar grafting with the visual advantages to be gained from a perforating central button, and considered it especially useful in heavily vascularized or otherwise badly complicated corneas.

Such an ingenious type of corneal graft has an unusual appeal in seeming to offer relative safety for very large lamellar replacement of opaque and diseased corneas, plus the visual advantages of a small, full-thickness button. Its usefulness would appear to apply to extensively scarred or highly vascularized corneas, such as may result from old penetrating ulcers, from extensive chemical burns, from previous unsuccessful penetrating grafts, or indeed wherever a very large graft is needed. Its greatest usefulness, however, would appear to be in aphakic eyes, whether the graft is needed for bullous keratopathy, or for other corneal opacification or irregularity resulting in a painful

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cornea. Here, in particular, the mushroom graft would appear to offer greater safety, especially from the danger of extensive vitreous loss, plus a penetrating central button for better vision.

The larger healing area seems to offer intriguing possibilities for quicker and more secure sealing of the wound and therefore quicker mobilization of the patient. It may also offer an interesting opportunity for the study of the healing process in grafts, and possibly a safe place for use of preserved corneas, which is demonstrated to be successful in lamellar grafts.

The technique of mushroom grafting, using ordinary instrumentation appears formidable. Franceschetti devised a mechanical cutter for the donor graft which is certainly ingenious but apparently rather difficult to use and certainly traumatic to the tissue, especially the corneal endothelium, which Stocker has pointed out to be of primary importance in the healing of corneal grafts. Stocker, in 1958, markedly furthered the cause of the mushroom graft with a technique which he devised, using marking calipers and multiple trephines. However, this technique, with which he has had considerable success, appears to require undue technical dexterity and is likely to result in imperfect matching of the graft to the recipient bed. However, it rightly emphasizes protection of the endothelium of the penetrating button.

My technique, employing a new instrument system, should make the operation easy for any reasonably experienced ophthalmic surgeon. It produces perfectly fitting donor grafts and recipient beds, and spares the endothelium of the donor cornea any undue trauma since it is subjected to no direct contact during performance of the operation.

The instrument system (figs. 1, 2 and 3) uses combined mechanical and suction fixation, calibrated outside guards on the trephines which are made with the bevels on the inside, and guiding devices for placing the trephine cuts in both donor and recipient corneas. These make possible easy achieve-

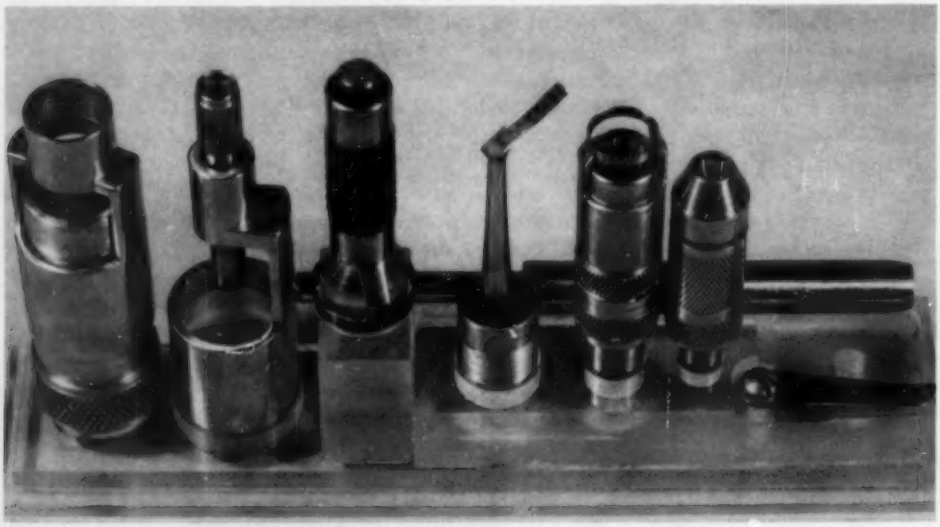

Fig. 1 (Roberts). Mushroom corneal graft instrument set mounted on plastic carrier. (Left to right) Fixing block and trephine guide, fixing cylinder and guide, "cookie cutter" 15-mm. trephine, 10-mm. trephine with guide for 5.0-mm. trephine, 5.0-mm. trephine. (Rear) Suction cylinder for fixation on recipient cornea.

ment of accurately fitting grafts and donor beds, as has been demonstrated in many experimental animals and eye-bank eyes and in initial clinical trials.

While lamellar and penetrating cuts of any reasonably similar size might be done, I have found it most convenient and feasible to use an instrument system which includes a 10-mm. trephine to make the outer cut for the lamellar portion of the graft, and a 5.0-mm. trephine for the inner or penetrating portion of the graft. This has made it possible to cover almost the entire cornea without getting into loose conjunctival tissue, as may so readily be done with a larger graft, and has also permitted an adequate penetrating window with a ledge which is sufficiently large and easy to work with outside this window. If, for any reason, larger grafts of 11 or 12 mm. are desired, the instrument system can readily be made to fit such needs.

The recipient eye is first prepared (figs. 4 and 7). The outside guard on the 10-mm. trephine is set for the desired depth of the lamellar cut. This cut is made either using the trephine alone or using it over a close-fitting hollow, central, cylindrical core with a concave perforated footplate which is adapted to the corneal curvature and which is placed against the corneal epithelium. This guiding core is attached to light suction in order to provide a guide for the trephine and to permit no creep in turning the large trephine, thus assuring a perfectly round cut.

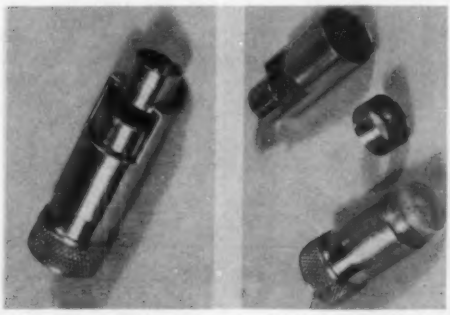

Fig. 2 (Roberts). Suction fixing base for mushroom corneal graft, with steel-toothed fixing ring and trephine guide, separate and assembled.

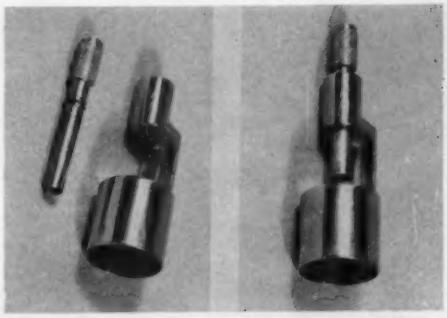

Fig. 3 (Roberts). Fixing device for dissection of endothelial-surfaced, lamellar ring around penetrating core of mushroom graft, separate and assembled.

After making this initial cut with the 10-mm. trephine, I have found it convenient to use the unsharpened fixing ring with the guiding cylinder, into which the five-mm. trephine will fit, to make a central five-mm. cut of the same depth as the outer cut. Following this, the lamellar dissection of the outer layers of the recipient eye is done, using Paufique, Took, or other dissecting knives which may be suitable for the purpose. The additional central cut with the five-mm. trephine permitted better evaluation of the thickness of the badly diseased corneas used in the initial tests. By making it possible to work from the center as well as from the periphery, lamellar dissection is easier.

Following removal of the lamellar layer, the recipient eye is completed for reception of the graft by using the five-mm. trephine within the guiding ring which fits into the 10 mm. cut, and cutting through with a full penetrating cut to remove the central button. If necessary this cut is completed with scissors. In the actual performance of the operation, it is preferable to leave the final removal of the penetrating five-mm central button until the graft has been prepared. This leaves the recipient eye in a safer condition while the graft is prepared.

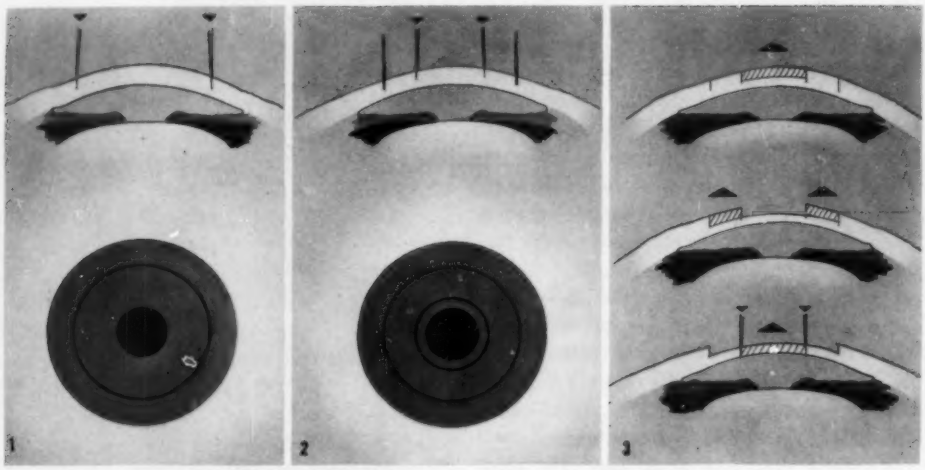

Fig. 4 (Roberts). Preparation of recipient eye. (1) Marking depth and extent of lamellar cut with 10-mm. trephine. (2) Marking central depth with 5.0-mm. trephine. (3) Lamellar dissection and penetrating cut with 5.0-mm. trephine.

PREPARATION OF THE GRAFT (figs. 5 and 7)

In preparing the mushroom graft itself, the entire anterior segment of the donor eye is removed, using a large 15-mm. trephine made in the form of a "cookie cutter," thereby making possible better visualization of the cut and placement of the trephine for marking and partially excising the anterior segment; excision is completed with scissors. This anterior segment is then peeled off the anterior uvea, usually freely but, if necessary, by gentle separation with a spatula.

This excised anterior segment is then placed, concave or endothelial side up, on the

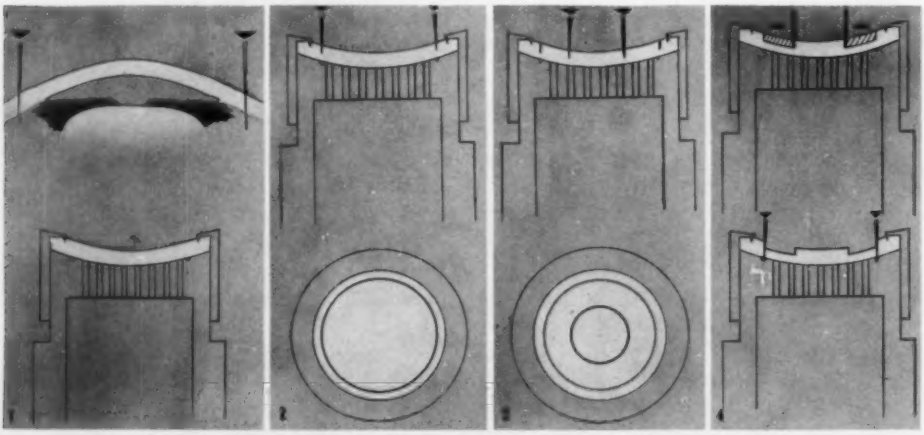

Fig. 5 (Roberts). Preparation of graft. (1) Excision of anterior of donor eye and placing, endothelial side up, on fixing block. (2) Marking of lamellar depth and extent on graft (10-mm. trephine). (3) Marking of penetrating button (5.0-mm. trephine). (4) Dissection of lamellar doughnut around fixing cylinder.

fixing block, a cylinder with a concave upper surface and the curvature of the human cornea, and with multiple small perforations leading to the hollow core. The fixing block is connected to a base and suction outlet to permit pulling suction on the epithelial surface of the cornea to fix it firmly to the surface of the fixing block (fig. 2).

The anterior segment of the donor eye is centered accurately, the suction is turned on, and fixation is then made absolute by pulling down over the upper end of the block and the donor cornea a stainless steel ring with downward-pointing, small teeth, which fix into the small scleral rim outside the donor cornea around its entire circumference and permit no slipping of the eye on the fixing block during further dissection.

A trephine guide is then slipped over the

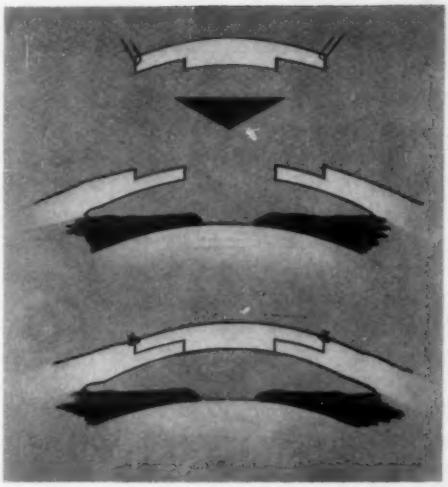

Fig. 6 (Roberts). Placing of graft in recipient cornea.

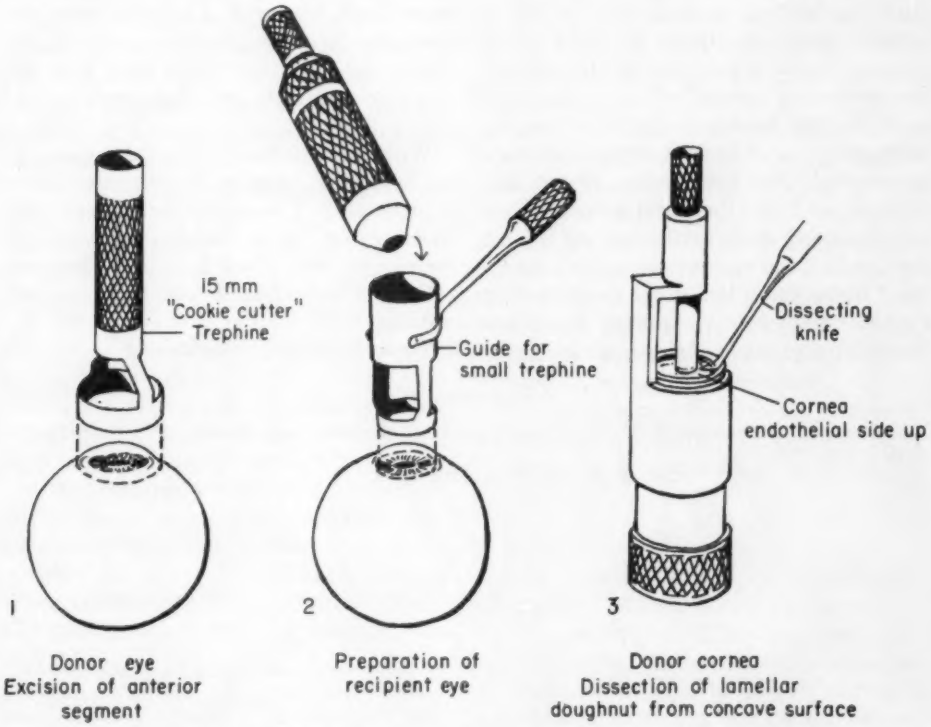

Fig. 7 (Roberts). Details of instrumentation in mushroom corneal graft operation.

cylindrical fixing block so that the trephines, which fit within this guide to close tolerances, are held perfectly perpendicular and centered above the endothelial surface of the excised anterior segment of the donor eye. The 10-mm. trephine is set for the desired depth, as estimated from the depth of the lamellar cut made in the recipient eye and the normal corneal thickness, and the trephine is turned to make this initial cut.

The 5.0-mm. trephine, with the guide set to the same depth, is then inserted through the same guide, which centers it perfectly within the 10-mm. cut, and a 5.0-mm. cut is made into the endothelial surface, leaving the endothelium on the penetrating button completely untouched by instruments. The trephines are removed.

A thin, unsharpened cylinder, which is essentially a thin-walled, unsharpened trephine threaded to fit its guide (fig. 3) is screwed down into the cut of the 5.0-mm. trephine to provide protection for the walls of the penetrating button and to provide even more absolute fixation during the dissection of the doughnut of lamellar tissue which must be removed from between the 10-mm. and 5.0-mm. cuts. This dissection is then carried out, dissecting from the 10-mm. cut toward the center, using appropriate knives; the inward dissection is limited by the protecting cylinder. Since both the guiding device for fixing cylinder and the fixing block itself may be readily rotated without moving the position of the operators hands, accurate and uniform dissection of the endothelial-surfaced doughnut of corneal tissue is possible, with minimum inconvenience to the operator.

After the doughnut-shaped donor ring of tissue is removed, the fixing 5.0-mm. cylinder is removed and the 10-mm. trephine is again applied through its guide to complete excision of the graft from the excised anterior segment of the donor eye. The guide is set to permit a penetrating cut of the 10-mm. trephine, which is made over the fixing block. There is a groove at the 10-mm. circle of the fixing block into which the trephine cuts, thus avoiding dulling the blade.

Upon completion of the penetrating cut, the trephine and the outer scleral rim with its metal fixing ring are removed, leaving the completed graft endothelial side up on the fixing block. The graft is removed from the block and inverted into the completed recipient bed and sutured into place with appropriate sutures to give firm fixation (fig. 6).

With the described guides, these maneuvers have been found to be relatively simple to accomplish. The most difficult part of the operation now is the lamellar dissection in the recipient eye, which is no different from a lamellar dissection in any badly scarred cornea.

Department of Ophthalmology.

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EXPERIMENTS ON LENS REGENERATION IN RABBITS*

I. Lens regrowth after extracapsular extraction with keyhole iridectomy

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August H. Wells, M.D., and Robert L. Katz
Cleveland, Ohio

Regeneration of the crystalline lens in the mammalian eye was first reported by Cocteau and Leroy d'Etiolle in 1824. After removal of the lenses in six rabbits, they found in one animal, five and one half months later, "that the capsules were perfectly transparent and contained lenses as voluminous and as consistent as those which had been extracted."[1]

During the following years of the 19th century other investigators confirmed these findings.[2-12] In the majority of their experiments the regenerates were small and only an occasional one reached the full size of a normal lens. Other workers[13-16] obtained no regenerates at all and denied the possibility of lens regeneration in mammals. Recently Russian and English authors obtained lens regenerates after implantation of embryonic tissue into rabbit eyes.[17-19]

This report concerns the spontaneous regeneration of the rabbit lens after extracapsular extraction.

Methods and Materials

Adult rabbits were used without preference as to race or sex. Bicillin injections were given on the day before surgery. Anesthesia was obtained by intraperitoneal Pentothal injection. Great care was taken to perform surgery under strictly sterile conditions.

After preparing a fornix-based conjunctival flap, the anterior chamber was opened by a corneoscleral section reaching from the 9- over the 12- to the 3-o'clock position. A keyhole iridectomy was performed in the 12-o'clock position and the anterior lens capsule was opened by an incision in the horizontal meridian. In some eyes this incision was performed in the perpendicular meridian. The lens material was removed as completely as possible by means of a small wire loop. The wound was then closed with gut sutures and the iris carefully replaced. The conjunctival flap was pulled over the wound and anchored with wing sutures at the 5- and 7-o'clock positions at the limbus. Bacitracin ointment was applied daily for the first 10 postoperative days.

Intracapsular extractions were performed on 10 rabbit eyes with the aid of alpha chymotrypsin. Otherwise the technique was identical with the one given for extracapsular extraction.

Of 52 eyes from which the lens was extracted extracapsularly, nine had to be discarded because of severe intraocular inflammation. The remaining 43 eyes of this group and the intracapsularly extracted eyes were repeatedly examined under the slitlamp. In order to determine the final size of the lens regenerates, the eyes were enucleated at different intervals after surgery, halved in an equatorial plane and photographed.

Also enucleated were eyes which showed some early regeneration but which failed to continue regenerative growth for as long as three months.

Results

None of the intracapsularly extracted rabbit eyes showed signs of lens regeneration.

Only one of the 13 extracapsularly extracted eyes that were enucleated between one week and one month after surgery showed a sizeable regenerate (fig. 1). Of the 19 eyes that were enucleated between six weeks and four months postoperatively, 11 showed a

* From Western Reserve University School of Medicine and the University Hospitals of Cleveland, Department of Surgery, Ophthalmology Service. This study was supported by research grant B-2678 of the National Institutes of Health, Bethesda, Maryland.

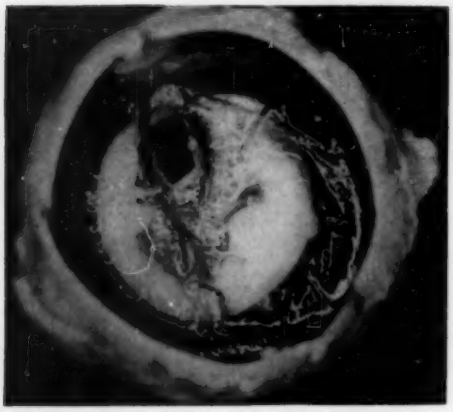

Fig. 1 (Binder, Binder, Wells and Katz). Small lens regenerate four weeks after extracapsular lens extraction. Anterior half of globe as seen from behind. Fixation in Zenker's fluid.

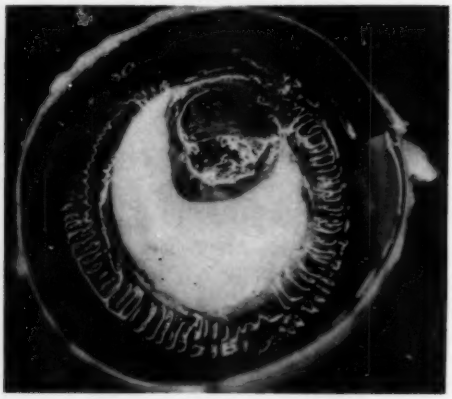

Fig. 3 (Binder, Binder. Wells and Katz). Lens regenerate four months after extracapsular lens extraction. Anterior half of globe as seen from posterior. Fixation in Zenker's fluid.

definite but small regenerate (fig. 2), while one other eye of this group harbored a large regenerate (fig. 3). All of the 11 eyes which were enucleated between five to 12 months after surgery had regenerated sizeable portions of their lenses. The two largest regenerates had grown for six and seven months respectively, and showed regular sutures on their anterior surfaces (fig. 4).

Lens regrowth started, as a rule, between two to four weeks after surgery at the lower equator of the lens capsule. A small irregular lump of clear tissue formed and enlarged gradually along the equatorial zone, achieving a more or less complete ring shape. During the following weeks the central portions filled in, assuming a shape that depended upon the adhesions of the capsule leaves. In eyes in which the anterior capsule was opened by a horizontal section the scar led to a horizontal delineation of the upper edge of the regenerate (fig. 3). When a perpendicular incision had been performed, the regenerate was divided, resembling the letter "V" (fig. 5).

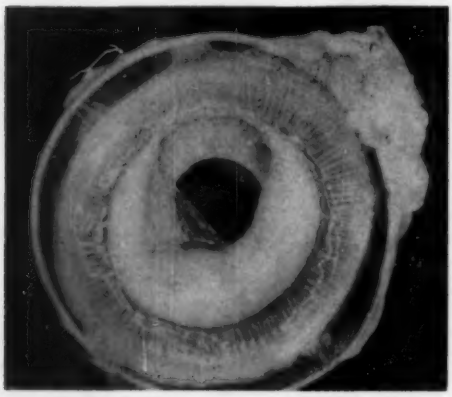

Fig. 2 (Binder, Binder, Wells and Katz). Horseshoe-shaped lens regenerate four months after extracapsular lens extraction. Anterior half of globe as seen from posterior. Fixation in Zenker's fluid.

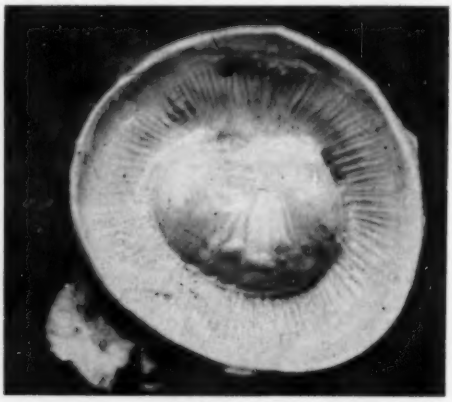

Fig. 4 (Binder, Binder, Wells and Katz). Lens regenerate seven months after extracapsular lens extraction. Anterior half of globe as seen from posterior. Fixation in Zenker's fluid.

The optical qualities of the lens regenerates were usually imperfect since most of them did not fill the pupillary area completely. While some portions of the regenerate proved to be clear, other segments of the same lens were of irregular optical density and of a vacuolar nature which obstructed the view of the fundus. Large regenerates were clearer than small ones.

In many of the eyes which failed to produce lens regenerates after several months, an abundance of fibrin was noted in the anterior segment during the early postoperative course which led to obliteration of the capsule sac. A semitransparent silky membrane could be seen in the pupils of these eyes.

Discussion

After the fibers which grow from the posterior lens epithelium have filled the space of the primary lens vesicle during an early embryonic period, further growth of the lens is derived from cells that lie just anterior to the equator. They elongate until their tips meet in the area of the anterior and posterior lens poles to form sutures. This regenerative activity continues throughout life.

The normal lens pattern results from confinement by the uninjured intact capsule. The lens epithelium continues to form new fibers after the lens capsule has been opened, but there is no confining area to shape and compress them.

Fig. 5 (Binder, Binder, Wells and Katz). V-shaped lens regenerate following extracapsular lens extraction after perpendicular incision of the anterior capsule. Anterior half of globe as seen from posterior. Fixation in Zenker's fluid.

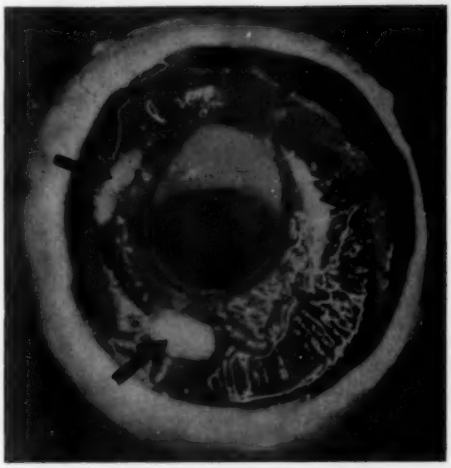

Fig. 6 (Binder, Binder, Wells and Katz). Three small isolated areas of lens regeneration four months after extracapsular extraction (arrows). Anterior half of globe as seen from posterior. Fixation in Zenker's fluid.

It is obvious from previous histologic reports (Gonin,[10] Randolph,[12]) and from our observations, that regrowth of the lens starts in the equatorial zone. If the leaves of the capsule are in loose apposition, the enlarging new lens masses will gradually fill in the available space. Deformities will depend upon the manner in which the wound in the anterior capsule leaf healed and to what extent permanent adhesions formed.

Fibrin, always present in normal wound healing and particularly abundant in traumatized rabbit eyes, may lead to obliteration of the capsule which is often followed by a permanent fibrous closure of the capsule sac. Under these circumstances multiple isolated areas of lens masses form, which are apparently unable to separate the capsule leaves and regeneration seems to be arrested (fig. 6). This relationship was first recognized by Middlemore and later by Textor, Milliott and Gonin.

The fact that lens regeneration starts most actively at the 6-o'clock position of the lens equator may be explained in different ways.

Lens material left behind during surgery will gravitate to this position and will enlarge by hypertrophy. This was demonstrated by Backhausen, Gonin, and Randolph. It is not known whether these remainders are also able to grow by cell division. They provide for mechanical separation of the capsule leaves and allow for unobstructed continuation of the growth which originates from the capsular epithelium of the equator.

While the classic experiments of L. S. Stone (1940-1959[20]) have shown amphibian lens regeneration to depend upon the presence of the iris, no such relationship has been established in mammalian lens regrowth.

Conclusions

1. When the lens was extracted intracapsularly, no lens regeneration took place.

2. After extracapsular extraction with keyhole iridectomy, lens regeneration was observed as early as two weeks after surgery. The largest regenerates were obtained six and seven months after surgery, respectively.

3. While some of the bulk of the regrowth is formed by the lens material left in the capsule after surgery, most of it is derived from the capsular epithelium just anterior to the equator. If the capsule healed without adhesions, the regenerate reached a size and form that approximates that of a normal lens. If adhesions of the capsule leaves were extensive or complete, deformed and small regenerates were found, or regrowth was suppressed completely.

4. It is our opinion that lens regeneration in rabbit eyes occurs in two phases: (a) hypertrophy of lens fibers remaining in the capsule after surgery; (b) continued formation of lens fibers from the lens capsule epithelium at the equator. The latter probably is the more important one.

5. All lens regenerates were optically imperfect.

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A NEW TEST FOR THE VIABILITY AND VITALITY OF CONJUNCTIVAL AND CORNEAL EPITHELIAL CELLS*

Methylene blue decolorization

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By viability, we mean the capacity for biologic survival because of the presence of life or "bios" in any structure and by vitality, the amount, quality and activity of that capacity for survival. In this investigation, we will deal particularly with conjunctival and corneal epithelial cells.

Life or "bios" is something mysterious and invisible, directly that is, with all the known research tools that we have. It is as yet unknown how to visualize directly the "bios" in a cell or noncellular structure, much less to determine its quantity. The most that we can do at present is to detect life indirectly by its manifestations. Of these biologic manifestations, we believe that metabolism is one of the most basic and essential. It is the foundation upon which the cell carries out its other vital functions. Among these manifestations, which are also considered as indices of viability itself, may be mentioned the following: (1) Survival, growth and reproduction, as are applied in tissue cultures;[1,4] (2) consumption of oxygen and raw materials, as glucose;[2] (3) excretion of end- or by-products of metabolism, as lactic acid; and (4) the normal electrophoretic patterns of "live" proteins.[3]

A perennial problem that confronts the keratoplasty surgeon is how to determine the viability and vitality of corneal grafts before transplantation. That this problem has disturbed many ophthalmic surgeons is shown by the many procedures which have been used as indices of the viability and vitality of corneal grafts.

We have long been interested in what happens to the bared sclera after pterygium operations. I wanted to know just how fast the epithelium grows over the wound and considered the use of methylene blue for this. To verify that the blue dots seen by biomicroscopy in the conjunctiva were really epithelial cells—sections were taken and examined under the microscope. It was observed that decolorization of the epithelial cells (blue dots) took place after they had stood for some time. This was the clue which suggested certain concepts of biologic staining and decolorization of cells based on their viability and vitality. Experiments were then set up to prove our hypotheses.

Our concepts

1. Living cells stain and decolorize differently from dead cells.

2. Various kinds of healthy living cells stain differentially.

3. Living cells of the same kind and of varying degrees of vitality stain and decolorize differentially. The rate of decolorization of cells is directly proportional to their vitality.

Experimental data

1. Six small pieces of conjunctiva excised from apparently normal eyeballs were treated in the following manner:

a. Stained directly in 0.25-percent methylene blue for five minutes. (The percentage and the time of contact were arrived at after making several trials.)

b. Stained as in (a) and placed in 5.0-percent formalin for five minutes.

* From the Section of Ophthalmology, Department of Eye, Ear, Nose and Throat, UP-PGH Medical Center. This study was aided by a research grant from the University of the Philippines and the National Science Development Board. Presented at the first annual meeting of the Philippine Ophthalmological Society, October, 1959.

c. Placed in 5.0-percent formalin for five minutes and stained as in (a).

d. Placed in denatured alcohol for five minutes and stained as in (a).

e. Heated in an open flame and stained as in (a).

f. Frozen in CO_2 snow and stained as in (a).

All of these pieces of excised conjunctiva were rinsed in normal saline solution and mounted on slides with normal saline solution and observed under the microscope.

The fresh untreated and stained pieces of conjunctiva stained in different degrees in different areas, that is, deeper in some parts and lighter in others. The lighter areas decolorized in about 15 to 20 minutes, and the deeper staining areas in about 30 to 40 minutes. This decolorization occurred in the center, leaving a stained periphery (corresponding to the site of the cut). All the treated pieces of conjunctiva invariably stained a little deeper than the fresh specimen and decolorized very little, if at all, even after two to three hours of observation.

2. Deliberate injury to conjunctiva by cross incisions (definite figures in order that they could be detected under the microscope) and pinching with forceps and then staining with 0.25-percent methylene blue for five minutes. The injured sites and the areas immediately around them stained a little deeper than the rest and decolorized very slowly or not at all.

3. Stored conjunctival tissues (donor eye is liquid paraffin at 4°C. for five days) stained a little deeper with 0.25-percent methylene blue for five minutes and the patterns of the cells were distorted. They decolorized very slowly in a few areas and not at all even after three hours in most cases.

4. Repeatedly stained fresh conjunctiva, which had previously decolorized after being restained as described, decolorized after the second staining although more slowly than the first (about two times longer) and did not decolorize any more after a third staining.

5. Filter paper stained in the same way did not decolorize significantly even after three hours of observation (mounted in normal saline solution).

Because of the ease with which it could be obtained, we did most of our experiments on conjunctival epithelium. However, we also performed some experiments on corneal epithelium. Our observations were as follows:

1. Very fresh corneal epithelium from an apparently normal cornea, stained as the conjunctiva, was compared with corneal epithelium, stained in the same way, from a five-day-old donor eye. The former decolorized very fast (15 to 20 minutes); the latter very slowly or not at all.

2. Repeated staining of fresh corneal epithelium which had been decolorized after being stained did not show any significant decolorization.

We tested cornea preserved in glycerine according to King's method with the described procedure. There was no decolorization, showing that at least the epithelium is not viable. This seems to support the negative results of tissue cultures done by King.[5] We also studied fresh corneal stroma; this showed negligible or no decolorization.

We recorded this phenomenon of methylene blue decolorization as an index of viability and vitality of corneal and conjunctival epithelium quantitatively by spectrophotometry, using the Beckman Model DU spectrophotometer set at 668 millimicra, the maximum absorption of methylene blue (fig. 1).

Decolorization of stained conjunctival and corneal epithelium was observed only when the stain used was methylene blue. We tried such other vital stains[6] as safranin, trypan blue, cresyl violet, Janus green B, Nile blue, crystal violet, neutral red, and so forth, using the same concentration and time of staining; the phenomenon was not demonstrated.

Discussion

Our experiments established a definite correlation between decolorization of cells stained with methylene blue and their via-

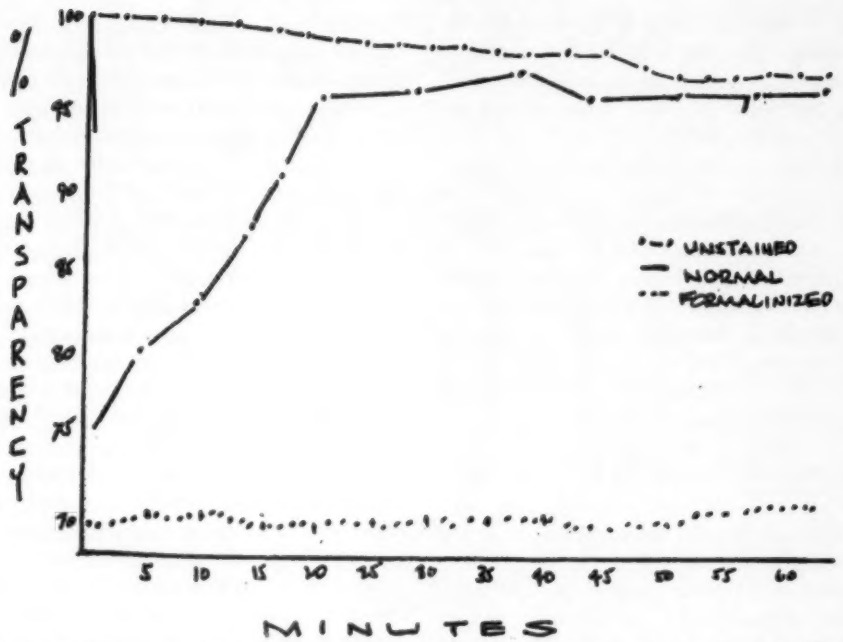
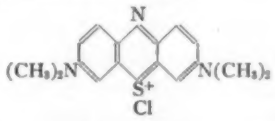


Fig. 1 (de Ocampo and Fojas). Spectrophotometric graph. Percentage of transparency of differently treated specimens of conjunctival epithelium graphed against time. The uppermost line represents an untreated specimen which shows very slight decrease of transparency as time progresses. Compare the increase of transparency with time of the normal-stained conjunctival epithelium with the almost constant degree of passage of monochromatic light through the formalinized and stained specimen.

bility and vitality. Dead cells (those treated with formalin, alcohol, heated and frozen) do not decolorize, while living cells do. A direct relationship is also shown between the rate of decolorization and the vitality of the cells—the less vital the cells (injured and stored tissues), the slower the decolorization.

Methylene blue is a basic dye with the following structural formula:



It is widely used as a vital stain and is known for its unstable nature. It has been observed that methylene blue slowly decolorizes on exposure to light and under lack of oxygen. By reduction also (for example, after the addition of sodium hyposulfite), methylene blue is transformed into a reduced (colorless) form. This property of methylene blue and the fact that it is an artificial hydrogen acceptor have made it useful as an indicator for certain respiratory enzyme systems.[7]

The relatively faster rate of decolorization in our experiments and the nondecolorization of stained filter paper eliminates the possibility of spontaneous decolorization. Physical diffusion is beyond consideration because decolorization is invariably observed in the central areas of the excised tissues and the periphery remains stained or decolorizes very much more slowly.

Now, the question may be asked: What is the possible mechanism of this observed decolorization? Since the speed of decolorization is directly proportional to the vitality of the cells, we must consider either a biologic or biochemical mechanism for this process. The property of active ingestion and expul-

sion or digestion or lysis of foreign substances (as any dye inside the cytoplasm or nuclei) is observed in reticulo-endothelial cells. Epithelial cells are, however, not endowed with this faculty.

The rate of decolorization of methylene blue by viable and highly vital corneal and conjunctival epithelium is relatively rapid so that an actual reduction of the dye must be considered. This stain has long been known to be an artificial hydrogen acceptor in the dehydrogenase reaction of the respiratory enzyme system, and having thus accepted the hydrogen it is reduced to its colorless form. The reaction follows:

$$\text{Substrate: H} + \text{methylene blue} \xrightarrow[\text{dehydrogenase}]{} \text{substrate} + \text{Mb:H (colorless)}$$

There are several dehydrogenases in the intracellular enzyme systems responsible for respiration. In their presence certain substrates (fumaric acid, succinic acid, and so forth) which are found inside the cells get rid of their hydrogen elements, which are carried to so-called hydrogen acceptors. Methylene blue can be substituted for these hydrogen acceptors. We have not tried to identify the particular dehydrogenase in our tests.

While respiration is going on inside the cells, there is a continuous transfer of hydrogen ions by hydrogen carriers to hydrogen acceptors. If this is responsible for the decolorization of methylene blue in our experiments, then it is an indirect indication of active respiration in the cells, because decolorization would mean the transfer of hydrogen in the presence of dehydragenases and its acceptance by methylene blue. Hence, the less vital the cells, the less the respiration, the less hydrogen transfer, and thus the slower the decolorization of methylene blue. Dead cells do not respire, so there is no hydrogen transfer and thus no decolorization in them.

There is need of proving the presence of and identifying the substrate and the specific dehydrogenase present in human conjunctival and corneal epithelial cells. We shall investigate this in the future. However, we have presently shown an objective, direct, qualitative and quantitative correlation between decolorization of corneal and conjunctival epithelial cells stained with methylene blue and their vitality and viability. That methylene blue causes injury to the cells is shown by the slower decolorization, and finally no decolorization, of restained tissues which had previously decolorized.

In this report, we have dealt particularly with the epithelial cells of the conjunctiva and cornea. We have made parallel studies using the corneal endothelium with similar results. On the other hand, our observations show very negligible or no decolorization even in fresh specimens of corneal stroma. This could mean that the dehydrogenases are not present or are minimal in the stroma.

We believe that methylene blue decolorization is a reliable index of the viability and vitality of corneal and conjunctival epithelial cells. We are using it as a tool to explore the different phases of the problem of corneal viability and its relation to keratoplasty and corneal diseases.

Summary

Experiments on sections of conjunctival and corneal epithelium show a direct relationship between their viability and vitality and the rate of decolorization when stained with methylene blue. The mechanism of this decolorization based on the enzyme system is discussed.

Conclusions

1. Methylene blue decolorization is a new, reliable and practical test for the viability and vitality of conjunctival and corneal epithelial cells.

2. The viability and vitality of the cornea should refer to its different parts—epithelium, endothelium, stromal cells, fibers and ground substance—and not to the whole cornea.

3. Methylene blue decolorization will serve as a useful tool to investigate the different

phases of the problem of conjunctival and corneal viability and vitality.

4. Our concepts of the indices of viability and vitality of the different parts of the cornea should be re-examined. Emphasis should be placed on metabolism and biologic survival rather than merely on growth and reproduction.

UP-PGH Medical Center.

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THE REGISTRY OF OPHTHALMIC PATHOLOGY: PAST, PRESENT AND FUTURE*

XVII Jackson Memorial Lecture

Lorenz E. Zimmerman, M.D.
Washington, D.C.

The name of Edward Jackson is famous to all of you. I feel somewhat chagrined that I have come to learn about this great man only during the past several years. Unlike the previous persons whom you have honored by your invitations to be Jackson Lecturers, I was not trained in ophthalmology. The Jackson name was not the "household word" to me that it was to them. As a matter-of-fact, until 1953, I knew very little about ophthalmology or of the great men who were responsible for this specialty's having attained the remarkable position that it has today. I feel very humble, therefore, in coming before you this morning. It is the organization which I represent that deserves this honor—not me personally. For this reason, I have chosen for my presentation this morning, "The Registry of Ophthalmic Pathology: Past, Present and Future." I do believe that the Registry and, particularly, the *Army Medical Museum* which made this Registry possible, share with such eminent clinicians as Edward Jackson an important place in the history of American Ophthalmology. Pathology was not one of Jackson's personal hobbies, but it is evident that he commanded the respect of the most prominent ophthalmic pathologists of his day. In reviewing the volume dedicated to him in honor of his 70th birthday, I was pleased to find in it papers by such men as Finnoff, Friedenwald, the Giffords, Goar, DeLong and Verhoeff, all of whom wrote on subjects relating to pathology of the eye. Moreover, Dr. Jackson was always intensely interested in education. He firmly believed that even the greatest of leaders have much to "learn through contact with

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* From the Ophthalmic Pathology Branch and Registry of Ophthalmic Pathology, Armed Forces Institute of Pathology. Presented at the 65th annual session of the American Academy of Ophthalmology and Otolaryngology, October 9-14, 1960, Chicago.

Fig. 1 (Zimmerman). The first home of the Army Medical Museum, 1862-1863. The Surgeon General's office was also housed in this building. (Neg. No. 32779.)

their inferiors." I trust, therefore, that he would not be displeased that I have selected this subject to kudize him this morning.

I propose, as the principal part of this Jackson Lecture, to review the development of the Registry of Ophthalmic Pathology and to tell you something of our present activities. Then I would like to speculate a bit about the future and to enlist your aid in planning for the future. This Registry belongs to you, and it is, at least in part, your responsibility not only to preserve its heritage but to nurture it in such a way that its usefulness to us and its ultimate value to our patients and for the Nation's health will be enhanced.

The Army Medical Museum

Before turning our attention to the Registry of Ophthalmic Pathology, I would like to review some of the history of the parent organization, the Army Medical Museum (figs. 1-7). The Medical Museum, approaching its first centennial, was founded on May 21, 1862, by the Surgeon General of the Army, Brig. Gen. William Alexander Hammond. The original purpose of the Museum was to

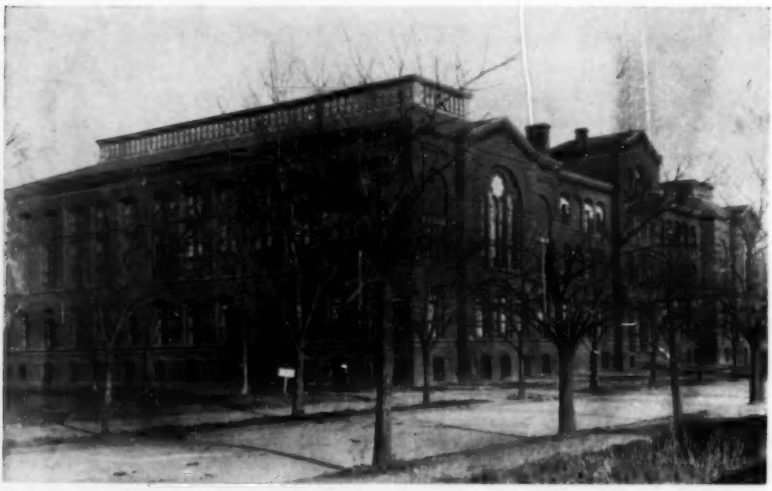


Fig. 2 (Zimmerman). The Army Medical Museum moved into this building in 1887, sharing the quarters with the Army Medical Library until 1955. This photograph was taken before World War I. (Neg. No. 415.)

house "all specimens of morbid anatomy, surgical and foreign bodies removed, and such other matters as may prove of interest in the study of Military Medicine or Surgery" obtained from the Civil War Battlegrounds. It is evident, however, that what General Hammond also had in mind was the development of a great graduate school of medicine in Washington, where Medical Officers of the Army would be kept abreast of new advances in Science and Medicine* (Leikind, 1954).

During the period 1862 to 1917, the professional staff at the Museum (figs. 8-11) demonstrated an extremely broad range of interests, which included such historically significant developments as Joseph Janvier Woodward's pioneer efforts in microscopy and photomicrography; Walter Reed's, James Carroll's, and Frederick Fuller Russell's investigations of the etiology, epidemiology, and prevention of infectious diseases; Daniel Smith Lamb's extended contributions to pathologic anatomy; and publication of the remarkably complete and extensively cross-indexed catalogues of the United States Army Medical Museum in 1866 (Surgical Section) and in 1867 (Medical Section).

During those early days, there seems to have been relatively little interest in ophthalmic histology and pathology, though, interestingly enough, we learn from the complaint of a Dr. L. E. Rauterberg addressed to the Senate Committee on Vivisection that the eye was the subject of some experimental work! "I have thus seen animals with eyes, sections of brain and other parts removed and kept in reserve for future experiments for a number of days and all for the verification and repetition of results obtained and published years ago." Fortunately, Major Walter Reed, then Curator of the Museum, was able to obtain testimony to the effect that Rauterberg's assertions of "the most inhuman and barbarous multilations of the dumb animal under the supervision and with the sanction of the United States Officers in Charge" were wonderfully distorted, inaccurate and false and that all animals experimented upon were under the influence of an anesthetic.

In the report of the Surgeon General for the fiscal year 1888-1889, there is a statement that 73 specimens of eyes showing disease or injury had been contributed by Dr. H. G. Noyes of New York City. Unfortunately, Dr. D. S. Lamb, pathologist of the Museum, was unable to locate any record of this contribution; he concluded that if Dr, Noyes' specimens were actually received, some disposition must have been made of them, of which no record is found. Lamb did acknowledge a contribution of 26 ophthalmic specimens from Dr. S. M. Burnett of Washington in June, 1889. The fate of these is also uncertain, for they are not in our present Registry of Ophthalmic Pathology, which includes only those specimens received during and since 1917.

While we are justly proud of the fact that the Registry of Ophthalmic Pathology is generally acknowledged as being the first of the Registries* established at the Army Medical Museum, we must recognize the fact that other specialty groups took active interest in the possibility of utilizing the Museum's facilities for specimen preparation, teaching and research long before the American Academy of Ophthalmology and Otolaryngology. Thus, we find in Dr. Lamb's history of the U.S. Army Medical Museum the following interesting quotation contained in a letter that Deputy Surgeon General John Shaw Billings, then the Director of the Museum and Librarian of the Surgeon General's Office, wrote to Dr. William Donally, a Washington dentist, on December 10, 1894:†

* This was the first organized medical research project for the diligent collection of pathologic specimens that was national in scope. Its objectives were to provide material for the training of Medical Officers, for research in methods to diminish morbidity and mortality of soldiers, and for preparation of the *Medical and Surgical History of the War of the Rebellion.*

* There are now 25 Registries in the American Registry of Pathology (table 1).

† See also Walton, J. R. (1895).

TABLE 1

REGISTRIES OF THE AMERICAN REGISTRY OF PATHOLOGY*

Registry	Sponsoring Society	Date	Registrars†
1. Ophthalmic Pathology	Am. Acad. of Ophthalmology and Otolaryngology	1921	L. E. Zimmerman, M.D.
2. Lymphatic Tumor	Am. Assn. of Pathologists and Bacteriologists	1925	R. J. Lukes, M.D.
3. Bladder Tumor	Am. Urological Association	1927	F. K. Mostofi, M.D.
4. Dental and Oral Pathology	Am. Dental Association	1933	L. S. Hansen, Capt., DC, USN
5. Otolaryngic Pathology	Am. Acad. of Ophthalmology and Otolaryngology	1935	S. H. Rosen, M.D.
6. Dermal Pathology	Am. Acad. of Dermatology and Syphilology	1937	E. B. Helwig, M.D.
7. Kidney Tumor	Am. Urological Association	1938	F. K. Mostofi, M.D.
8. Chest Tumor	Am. Assn. for Thoracic Surgery	1940	S. H. Rosen, M.D.
9. Neuropathology	Am. Assn. of Neuropathology-Am. Psychiatric Association	1942	W. E. Haymaker, M.D.
10. Orthopedic Pathology	Am. Soc. of Clinical Pathologists	1943	L. C. Johnson, M.D.
11. Prostatic Tumor	Am. Urological Association	1943	F. K. Mostofi, M.D.
12. Veterinary Pathology	Am. Vet. Medical Association	1944	F. D. Mauer, Lt. Col., V.C., USA
13. Gerontology	Gerontological Society	1945	G. H. Klinck, M.D.
14. Genito-Urinary Pathology	Am. Urological Association	1947	F. K. Mostofi, M.D.
15. Radiologic Pathology	Am. Coll. of Radiology-Am. Roentgen Ray Soc.-Radiologic Soc. of North Amer.	1947	W. L. Thompson, Col., MC, USA Ret.
16. Cardiovascular Pathology	Am. Heart Association	1948	W. C. Manion, M.D.
17. Endocrine Pathology	None	1948	G. H. Klinck, M.D.
18. Hepatic Pathology	Am. Gastroenterologic Society	1949	H. F. Smetana, M.D.
19. Leprosy	Leonard Wood Memorial	1950	C. H. Binford, M.D.
20. Nutritional Pathology	Am. Institute of Nutrition	1951	R. H. Follis, M.D.
21. Female Reproductive System	Am. Soc. of Clinical Pathologists	1952	R. D. Neubecker, M.D.
22. Gastro-intestinal Tract	Am. Soc. of Clinical Pathologists	1952	E. B. Helwig, M.D.
23. Pediatric Pathology	Am. Acad. of Pediatrics	1956	H. F. Smetana, M.D.
24. Forensic Pathology	Coll. of American Pathology	1958	E. H. Johnston, Maj., MC, USA
25. Testicular Tumor	Am. Urological Association	1959	F. K. Mostofi, M.D.

* Colonel J. M. Blumberg, MC, USA, is Scientific Director, American Registry of Pathology.
† September, 1960.

I have attempted in past years to call the attention of the dental profession to this institution (that is, the Army Medical Museum) as one which they should endeavor to make complete in all matters relating to the Pathology and treatment and diseases of the teeth and jaws so that it might be considered by them as their national collection of literature, specimens, apparatus, etc. to illustrate the history and condition of dentistry, just as other sections of the Museum and Library are considered to be their national collection by the physicians, surgeons, and specialists of the country; and it appears to me that more definite, useful and permanent results can thus be obtained than are likely to follow from an attempt to create a new Museum and Library devoted exclusively to matters of interest to the dental profession.

On September 16, 1895, Dr. Donally was one of a committee of the American Dental Association appointed to add to the dental exhibit in the Museum. As a result of the efforts of this committee the dental collection was much enlarged. The American Dental Association at its 36th annual meeting adopted a resolution formally recognizing the Museum and the Library as the National Library and Museum of the Dental Profession in the United States.

In his presidential address to the Washington Obstetrical and Gynecological Society on October 6, 1899, Dr. Thomas C. Smith chose to speak on the obstetric and gynecologic treasures available at the Army Medical Museum. He called the attention of his col-

Fig. 3 (Zimmerman). Main exhibit hall of the Army Medical Museum before World War I. (Neg. No. 746.)

leagues to the advisability of more frequently resorting to this storehouse of pathology and of considering the advantages to be derived from frequent visits to the Museum when they were preparing papers for oral presentation or for publication. In closing his address, Smith reminded his audience that it was their duty to add to the Museum's col-

Fig. 4 (Zimmerman). Same building as shown in Figure 2 at Seventh and Independence Avenue, S.W., after World War II, when it became the home of the Armed Forces Institute of Pathology. (Neg. No. 219761-2.)

Fig. 5 (Zimmerman). The Medical Museum of the Armed Forces Institute of Pathology presently occupies this building at Ninth and Independence Avenue, S.W. (Neg. No. 218702-2.)

Fig. 6 (Zimmerman). One of several exhibit halls in the present Medical Museum of AFIP. Part of the Ball collection (see fig. 20) is on display in one of these cases. (Neg. No. 59-4675-6.)

lections in every possible way and exhorted them not only to contribute specimens but to provide salient histories and results of such laboratory examinations as might have been made. Thus the value of Museum specimens would be enhanced, further investigation would be greatly facilitated, and the additional labor required of the contributor would be minimal. Amen!

In 1917, all pathologic specimens and other important acquisitions in the Museum were assigned consecutive accession numbers which are still in use today (fig. 12). While at first, the same series of accession numbers was used for such nonpathologic acquisitions in the Museum as wax models, old instruments, and photographs, it subsequently became the policy to reserve these accession numbers for individual case studies. Only one accession number is assigned to

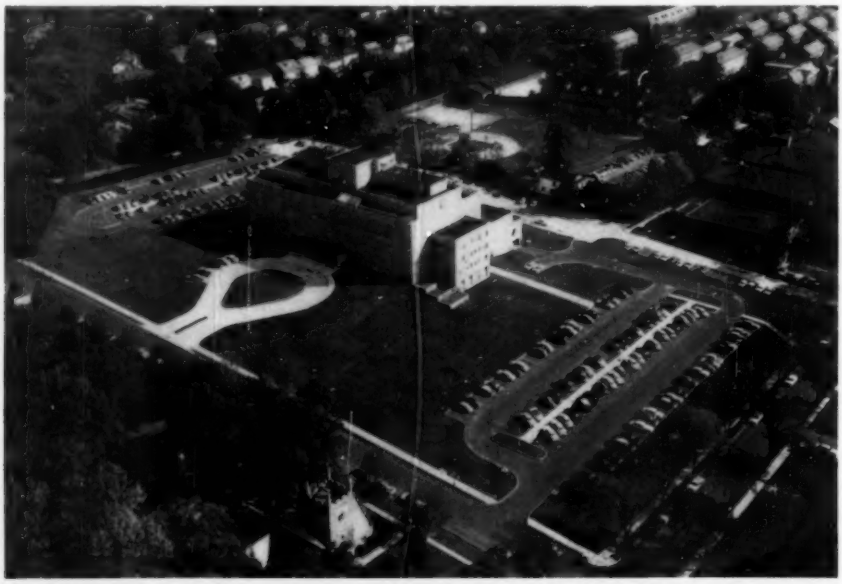


Fig. 7 (Zimmerman). Aerial view of new building of the Armed Forces Institute of Pathology on grounds of Walter Reed Army Medical Center. (Neg. No. 58-2917-26.)

Fig. 8 (Zimmerman). Army Medical Museum's first curator, Surgeon John Hill Brinton. (Neg. No. 58-7854-14.)

Fig. 9 (Zimmerman). Joseph Janvier Woodward, assistant curator and pathologist at Army Medical Museum from 1862-1881, was a pioneer in histopathologic technique and photomicrography. The photographic plate from which this picture was printed was made about 1880 (Edmonds, 1951). (Neg. No. 3659.)

Fig. 10 (Zimmerman). Major Walter Reed, MC, USA, fifth curator of the Army Medical Museum, 1893-1902. (Neg. No. 2546.)

Fig. 11 (Zimmerman). Dr. Daniel Smith Lamb, pathologist at the Army Medical Museum for more than 50 years, recorded the museum's history from 1862-1917. He also examined the oldest specimen (fig. 13) in our present Registry of Ophthalmic Pathology. (Neg. No. 57-13237.)

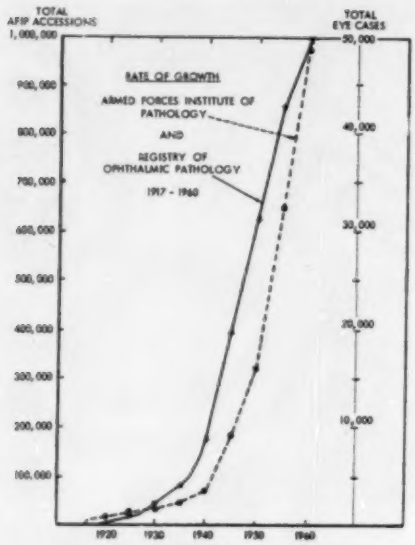


Fig. 12 (Zimmerman). Comparison of the period of accelerated growth of the Registry of Ophthalmic Pathology with that of the entire AFIP reveals the former began about five years before the latter. (Neg. No. 60-5610.)

any one individual.* Thus in the course of a lifetime, many biopsies and finally the autopsy of an individual will be filed under the same accession number.

It is of historical interest that the first new surgical pathology case contributed to the Museum in 1917 when the current series of "accession numbers" was begun was number "6." The first three acquisitions were temporal bones mounted for Museum display, purchased from the late Edgar B. Burchell of New York City. A series of photographs was assigned Acc. No. 4. The first autopsy case was that of an anencephalic fetus (Acc. No. 5). AFIP Acc. No. 6 is of special interest to us because it concerned a three-year-old Negro girl whose eye was enucleated at the Children's Hospital in Washington and contributed to the Museum by Dr. D. K. Shute on April 27, 1917. The specimen was examined by Dr. D. S. Lamb, who found an intraocular neoplasm which he misinterpreted as a "round cell melanotic sarcoma." The specimen was prepared for the Museum (fig. 13) and has been displayed under that erroneous diagnosis all these years! The tumor is actually a necrotic retinoblastoma that has invaded the choroid and extended posteriorly into the optic nerve and orbit.

Between 1917 and the beginning of 1922, only an occasional eye was submitted to the Museum for pathologic study. During this period, the total accessions, rose to about 18,000, a large proportion of which represented postmortem cases from the terrible influenza epidemic of 1917-1918. Among these 18,000 cases, only 18 eyes were included. This is fewer than we now receive in one average week. It is obvious, therefore, that pathologists at the Museum were not in a position to become expert in the field of ophthalmic pathology.

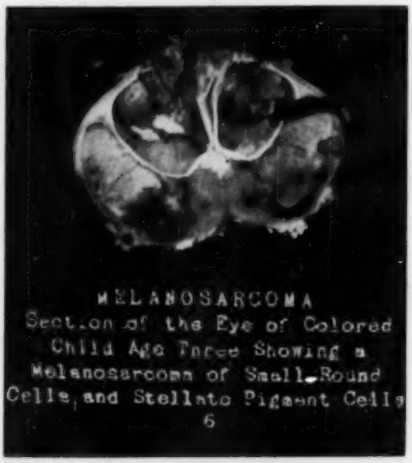


Fig. 13 (Zimmerman). This retinoblastoma, erroneously labeled a melanosarcoma when it was accessioned in 1917, represents the first surgical specimen contributed when the present series of accession numbers was begun that year. (AFIP Acc. No. 6.)

* By the end of the present calendar year the total number of accessioned cases on file at the AFIP will be approximately 990,000. Of these, about 50,000 are in the Registry of Ophthalmic Pathology, which includes 7,700 tumors, 4,600 cases of primary and secondary glaucoma, 11,700 eyes enucleated because of trauma, 900 congenital malformations, and 3,800 inflammatory lesions.

The Academy and the Museum

It has been impossible for me to obtain a completely clear picture of how the American Academy of Ophthalmology and Otolaryngology and the Army Medical Museum first came together, because the initial correspondence between officers of these two organizations has not been located either in Dr. Benedict's office at the Academy or in the Armed Forces Institute of Pathology. It is amply clear, however, that Dr. Harry Gradle (fig. 14), representing the American Academy of Ophthalmology and Otolaryngology, and Major George R. Callender (fig. 15), then the Curator of the Army Medical Museum, were the principal persons concerned with the organizational aspects of what we now call the Registry of Ophthalmic Pathology. In the minutes of the 1921 meeting of the Academy, Dr. Gradle made reference to a printed letter that was distributed to the membership of the Academy prior to the annual meeting. This letter, which is reproduced in Figure 16, describes action taken by the Council of the Academy to establish at the Army Medical Museum, a Section and Museum of Ophthalmic and Oto-Laryngologic Pathology. As Dr. Gradle pointed out, the Academy membership was in a position to contribute material which was lacking at the Museum and, on the other hand, the Army could supply the home for the Museum and the technicians necessary to prepare the specimens. Dr. Gradle's report recapitulating the union which had been effected between the Academy and the Museum was moved for acceptance by Dr. Nelson Black of Mil-

Fig. 14 (Zimmerman). Harry Gradle, M.D., to whom major credit is due for having conceived of a central laboratory and museum of ophthalmic pathology to be used for postgraduate training. (Neg. No. 60-5251.)

Fig. 15 (Zimmerman). Brig. General George Russell Callender, MC, USA, retired, who as a major serving as curator of the Army Medical Museum was responsible for the organization of an ophthalmic pathology laboratory and museum at the Army Medical Museum and for the subsequent American Registry of Pathology.

TWENTY-SIXTH ANNUAL MEETING, PHILADELPHIA, PA., OCTOBER 17-22, 1921

THE AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

My Dear Doctor:

At the June, 1921, meeting of the Council of the American Academy of Ophthalmology and Oto-Laryngology, it was decided to establish a Museum of Ophthalmic and Oto-Laryngologic Pathology. Is is obvious that a Society without permanent headquarters and without a staff of trained technicians could not make a success of such a project alone, since it would require a permanent location, a corps of trained technicians, a comprehensive method of filing and cataloguing specimens, and all of the other necessities of a museum. The Society, however, is in a position to supply abundant pathological material. A representative of the Council had approached the Surgeon General of the Army previous to this meeting and was offered the facilities of the Army Medical Museum for the establishment of such a collection as would be of most interest and value to Ophthalmologists and Oto-Laryngologists. The Army Medical Museum receives specimens of all varieties and has a large collection of Ophthalmic instruments, but only a very small collection illustrating Ophthalmic or Oto-Laryngologic Pathology. This institution has agreed to set apart certain space for the display of Ophthalmic and Oto-Laryngologic Pathology and to co-operate further by sending reports to donors of specimens, together with such photographs as it is found possible to take, both of the gross specimens and of any microscopical slides made therefrom. There is, however, no person at the Museum well qualified in Ophthalmic or Oto-Laryngologic Pathology. It is therefore considered necessary that all Ophthalmic and Oto-Laryngologic Pathologists who may be willing to assist in making diagnoses of the specimens prepared by the Museum be placed on a voluntary committee and asked to pass upon specimens which will be sent them for confirmatory diagnosis from the Army Medical Museum.

The following working plan is suggested in the hope that free and constructive criticism will be offered to the undersigned committee before final hard and fast rules are adopted:

(1) The name of this section of activities of the American Academy of Ophthalmology and Oto-Laryngology shall be "The Section of Pathology."

(2) The Museum collection shall be located in the Army Medical Museum at Washington, D. C.

(3) The administration shall be conducted by the Curator, Army Medical Museum, in consultation with a supervisory committee of the Academy. Any administrative matters involving the Army Medical Museum will require the approval of the Surgeon General, U. S. Army, as represented by the Curator, Army Medical Museum.

(4) All members of the American Academy of Ophthalmology and Oto-Laryngology are urged to send interesting specimens of Ophthalmic or Oto-Laryngologic Pathology to the Museum, together with as complete a protocol as possible, and to co-operate in every way to make the institution a success.

(5) The Army Medical Museum shall not be financially obligated. In case the amount of incoming material becomes so large as to require extra technical or clerical help, special arrangements therefor will be considered by the Academy. The minor expenses of printing, etc., amounting to not more than $100 per year, shall be borne by the American Academy of Ophthalmology and Oto-Laryngology.

The Surgeon General of the Army has signified his willingness to prepare a suitable collection of such material as may be available for exhibition at the annual meetings of the American Academy of Ophthalmology and Oto-Laryngology, the expenses of transportation and display to be borne by the American Academy of Ophthalmology and Oto-Laryngology.

Under the regulations of the Army Medical Museum the Pathological material is open for study to any qualified person, as may be determined by the Curator, and facilities are offered there for such study; a suitable laboratory and microscopes, together with access to the complete records of all specimens, are available during the hours the Museum is open.

Specimens sent in should be addressed as follows:

ARMY MEDICAL MUSEUM,
WASHINGTON, D. C.
Section of Ophthalmic (or Oto-Laryngologic) Pathology.

and should have the donor's name and address. A complete protocol of the case must be sent under separate cover, so labeled as to avoid confusion. Specimens for microscopic study should be placed in 10% formalin or Zenker's fluid as soon after removal as possible. After 24 hours, wash the specimen, change the fluid, and send it to the Museum in a tightly stoppered bottle within a stout carton.

MAJOR G. E. CALLENDER, M. C.,
Army Medical Museum,
Washington, D.

DR. H. S. GRADLE,
22 E. Washington Street,
Chicago, Ill.

DR. IRA FRANK,
104 S. Michigan Avenue,
Chicago, Ill.

Fig. 16 (Zimmerman). Photograph of the original letter distributed before the 1921 meeting of the Academy, advising the membership of the plans to establish a central museum of ophthalmic and otolaryngologic pathology at the Army Medical Museum.

waukee. The motion was seconded and carried. Thus we have, in 1921, the beginnings of the present Registry of Ophthalmic Pathology.

But, since neither trained technicians nor pathologists experienced in ophthalmic and otolaryngic pathology were available for this specialized work, a special committee would need to be developed to provide guidance. It was only natural that Gradle and Callender should turn to Dr. Frederick H. Verhoeff (fig. 17) of Boston for guidance. At about the time of the International Congress of Ophthalmology held in Washington, D.C., May, 1922, Verhoeff was called to the Museum to discuss the matter with them, at which time he suggested the formation of a Registry of Ophthalmic Pathology.* Verhoeff was asked to give the technicians of the Museum instructions as to the sectioning of eyes, which he did.

Some of Dr. Harry Gradle's remarkably farsighted thoughts, which coincided so well with those of Major Callender, Curator of the Museum, and General Ireland, Surgeon General of the Army, and which played such a major role in establishing the Registry of Ophthalmic Pathology, are contained in a lengthy letter which he wrote to Dr. Walter R. Parker, who was then president of the American Academy of Ophthalmology and Otolaryngology. This letter dated August 26, 1922, was written only 10 months after the Section and Museum of Ophthalmic Pathology were established at the Army Medical Museum. The letter read as follows:

My Dear Doctor Parker,

I believe that you are correct in recommending that only members of the Academy be intimately associated with the work of the Section on Pathology. However, it seems to me that the section has proven its value sufficiently in the short time that it had been in existence to justify an expansion that was in my mind when I first suggested the idea of the Section. An expansion that was necessarily dependent upon a small beginning and a cautious feeling of the way.

Fig. 17 (Zimmerman). Dr. Frederick Herman Verhoeff was the Army Medical Museum's principal consultant in ophthalmic pathology during the first two decades of the Registry's existence.

In order to show what has been accomplished and thus to lead to the bigger idea, allow me to recapitulate briefly. The Section on Pathology has been existent since last October. In that time we have received over 100 ophthalmic specimens and two oto-laryngologic. These have been worked through as rapidly as has been possible and consistent with good work and every one has been examined and diagnosed personally by Dr. Verhoeff (from now on, four of us are going to do the preliminary examining and then send the specimens to Verhoeff for final judgement). Every specimen is photographed in the gross and then worked-up in toto histologically. From this fairly large material, the Museum is preparing an exhibit for the Minneapolis Meeting that we hope will be creditable. But the material is not coming in the way it should. We do not expect material from you or Knapp or Verhoeff or the men with laboratories at their disposal. It should come from men in cities, not associated with an Institution that does ophthalmic pathology, and from the men in the smaller localities. To reach these men and impress upon them the value of sending in *all* of their material is the biggest task of the Section today, and mind you, all of this has been done without a cent of expense to the Academy or to any individual.

In order to increase the scope of the work and make the Museum the real center of Ophthalmic

* At this time the first of all national registries —the Codman Bone Sarcoma Registry—was less than two years old. Codman was then a friend and patient of Verhoeff's, and he often discussed with him his Bone Tumor Registry. Verhoeff probably obtained the term "Registry" from Codman (personal communication from Verhoeff).

Pathology, it is necessary to enlist a larger number of men as donors and to interest the teachers and leaders of the profession in encouraging such donations (at St. Louis, Dr. DeSchweinitz persuaded Dr. J. M. Ball to donate his entire pathological collection to the Museum). Further, oto-laryngologic pathology must be divorced from the ophthalmic and must be treated separately. To this end, I would like to propose to you the following scheme and, if it meets with your approval, then incorporate it in my report to the Academy on the activities of the Section on Pathology.

Let the Section on Pathology expand to a national body in the same way that the Board of Ophthalmic Examinations is national. Let it be under a committee of three, one appointed from each of the three national Ophthalmic Societies and each member to serve for three years. Each year, one member shall be retired automatically (after the end of the first three years) and his place shall be filled by a member appointed by the Society of which the retiring member was the representative. This committee shall have a fourth member who shall be the Curator of the Army Medical Museum. The committee shall have the power to act without referring to the parent body unless such action may be opposed to the policies of the parent societies. The expenses of the committee (purely nominal) shall be borne by the parent Societies, prorated according to the membership of the Society of the current year. Let the name of the loose organization be the American Museum of Ophthalmic Pathology (or what have you?) and the purpose, to found a central museum of ophthalmic pathology at the Army Medical Museum, utilizing for that purpose such pathological resources of the country as may be available. With such a formation established, several things could be accomplished. First, greater efforts could be made at obtaining material, as all local feeling would be eliminated and all of the members of all the national Societies would cooperate. Moreover, the aid of the 25 odd local Societies could be enlisted in securing material. Second, an exchange of unusual material could be arranged with the universities and Institutions doing ophthalmic pathology, to the greater advantage of all concerned. Third, all this would tend to stimulate a nationwide interest in the subject that has been sidetracked for the fascinating hunt of the dollar, namely ophthalmic pathology.

Now I come to some of the ideas that I am not willing to voice to anyone but you. After a few years, when sufficient material has been collected, it will be possible to assemble some three to eight of our nationally recognized ophthalmic pathologists in Washington or someplace else and give a 2 to 4 weeks course in ophthalmic pathology to such ophthalmologists as may desire it. Irrespective of what the price of such a course might be, there would be enough microscopes to go around. The attendance at the Fuchs lectures in Chicago, proved that. It will also be possible to make up study sets of 200 or more sections representing different phases of ophthalmic pathology, accompanied by complete descriptions, that could be sent around the country to places remote from institutions as loans for home study. I have two such sets out now and they are in constant demand. There are also a few other ideas that could be worked out, dependent upon the expansion of the Section on Pathology.

I am sorry to inflict this long a letter upon you, but I do not want to move in this matter without your advice. May I have that before the meeting in order that I can prepare the necessary report? We are running a special train out of here on Sunday nite, September 17, on the C. M. & St. P. I hope that you can join us on that as we expect a good crowd.

Cordially,
/s/ Gradle

Gradle, Verhoeff, and Callender then organized a panel of consultants to whom the Museum could refer difficult cases for descriptions and diagnoses. The panel included, in addition to Dr. Verhoeff, the chairman, the following men: Drs. Harry S. Gradle (Chicago), M. Feingold (New Orleans), William C. Finnoff (Denver), W. E. Camp (Minneapolis), and H. Barkan (San Francisco) (see Coupal, J. F., 1923).

As is so often the case with committees, there are always individuals who are eager to be on the committee but who fail to render service. The committee on Ophthalmic Pathology was no exception, as we learn in an interesting letter which Callender wrote to Gradle on February 27, 1926. Among other things, Callender stated:

I do not approve of adding any other person to this committee unless they are going to be active as a consultant pathologist. At the present time, I personally am reporting on a considerable number of specimens which are not difficult, sending only the difficult cases to Dr. Verhoeff. The result is we are up to date. Dr. ———— never reported on some of the cases he had and I never received replies from Dr. ————. Needless to say I am too busy to deal with people under these conditions and, therefore, I took up the work of handling the easiest specimens myself. I think it rather unfair that Dr. Verhoeff should do it all but that is the status and he is always extremely prompt in returning replies.

Subsequently a more satisfactory Advisory Committee of ophthalmologists who were exceedingly interested in the Registry of Ophthalmic Pathology and who rendered faithful service for many years was established.

In addition to Doctors Gradle and Verhoeff, the committee included Dr. Jonas S. Friedenwald (of Baltimore) (fig. 18) and Dr. Georgiana D. Theobald (of Chicago) (fig. 19) (Cornell, 1936).

It was very fortunate for Dr. Harry Gradle and the American Academy of Ophthamology and Otolaryngology that the pathologist who was Curator of the Army Medical Museum in 1921, Major George R. Callender, and the person who was then Surgeon General of the Army, Major General M. W. Ireland, were both anxious to alter the course of the Army Medical Museum. As Callender stated when he participated in the 1953 program of the Academy, the Army Medical Museum was rejuvenated by receiving an enormous amount of material from World War I. The staff of 1920 decided the Institution should become a live activity in pathology in addition to its function of collecting, studying, and reporting on the injuries and diseases of armed conflicts. Major General M. W. Ireland ably supported the decision and enabled the Museum to become an Institute of Pathology rather than a "pickle factory," as he had facetiously called it.

Fig. 19 (Zimmerman). Dr. Georgiana Dvorak-Theobald faithfully served with Verhoeff and Friedenwald on the ophthalmic pathology committee and was an important contributor to the Registry during its early days of rapid growth.

Fig. 18 (Zimmerman). Dr. Jonas Stein Friedenwald succeeded Verhoeff in the role of principal consultant to the Registry of Ophthalmic Pathology.

During the transition period which followed World War I, a follow-up program was established for tumors and for determining the residual pathology of diseases of military importance. It was at this time, when the Registry type of approach had already begun to be applied to cases on file at the Museum, that Dr. Harry Gradle approached Major Callender with his proposal to establish a central laboratory of ophthalmic and otolaryngic pathology.

The appreciation of the officers of the Academy for the active participation of the Army Medical Museum in the first annual meeting of the Academy following the establishment of the Section and Museum of Ophthalmic Pathology was expressed in letters to the Surgeon General of the U. S. Army. On September 25, 1922, Gradle wrote:

At the annual meeting of the American Academy of Ophthalmology and Otolaryngology that was just held in Minneapolis, the Army Medical Museum exhibited specimens of ophthalmic pathology, both gross photographs as well as microscopic slides. These specimens have been collected during the past year from the members of the Academy. The exhibit was largely attended and received great praise. It was one of the best public exhibitions that it has ever been my good fortune to see, an opinion that was concurred in by all of the pathologists at the meeting. I wish to take this opportunity of expressing to the Army Medical Museum through your office, the appreciation of the character of the work that has been done for the past year.

In view of the fact that this loosely bound union between the Army Medical Museum and the Section on Pathology of the American Academy of Ophthalmology and Otolaryngology has proved so successful, it seems advisable to endeavor to expand the field of activity. During the past year, about 100 ophthalmic specimens have been sent to the Museum. There should have been 5 to 10 times that number and even that would represent but a small amount of the ophthalmic pathological material that is wasted annually. By interesting a large number of men in the project, it would seem probable that a larger amount of material could be secured. In order to do this, I would suggest that the American Ophthalmological Society and the Ophthalmic Section of the American Medical Association, the other two National Ophthalmic Societies, be approached with the aim of securing their cooperation. The Academy has authorized me to make such advances, pending your approval. Should you approve of the suggested expansion, it probably would be better to handle the matter through the Academy. There is much to be gained by such cooperation. With the increased number of specimens that could be secured by proper publicity, through the three Societies, it would not be long before the Army Medical Museum would house the finest collection of Ophthalmic Pathology of any Institution. Such a collection would increase rapidly by arranging exchanges with other Institutions doing similar work and eventually would offer the greatest teaching possibilities that exist. In fact, the possibilities are nearly unlimited and if the standards, set by the work of this past year, are maintained (as I am sure they will be), there will be established a Mecca for ophthalmic pathologists. May I hear from you on this subject?

Again I wish to express the appreciation of the Academy of the work and of the exhibit of the Army Medical Museum, Section on Ophthalmic Pathology, and I shall take the opportunity of expressing that appreciation in person on my visit to Washington during the next month.

Very truly yours,
/s/ Gradle

On October 7, 1922, Dr. Walter R. Parker wrote to General Ireland as follows:

I have just finished my term as President of the American Academy of Ophthalmology and Otolaryngology, and wish to express to you my great appreciation of the generous arrangement you have made with the Academy for their pathological work. The exhibition in Minneapolis was a great credit to all of us, and I believe that this opportunity to make these specimens available for study will be productive of great results.

Dr. Gradle and his committee have been very active, and are as enthusiastic over the arrangements made with the Army Medical Museum as I am. Thank you many times.

With kindest personal regards.

Very sincerely yours,
/s/ Walter R. Parker

In the minutes of the 1923 meeting, Gradle reported that the committee on pathology had been working in a rather loose manner and unfortunately for some, "the greatest endeavor has been along the line of ophthalmic pathology, so that oto-laryngology has been treated in a rather stepmotherly fashion." He recommended that the Section on Pathology be divided into two separate committees, Ophthalmic Pathology and Oto-laryngic Pathology, since these represent so radically different fields that no one committee would be able to handle them properly. Gradle pointed out that the Section on Ophthalmic Pathology had endeavored to become nationalized in that the Academy had joined with the American Ophthalmological Society and the Section on Ophthalmology of the American Medical Association in endeavoring to establish a "National Museum of Ophthalmic Pathology" with headquarters at the Army Medical Museum. The plan which was approved at the 1921 meeting and which had been put into effect during 1922 was as follows: Ophthalmologists were requested to send in all of their specimens, not only those

that were rare or unusual, for, in order to have a complete collection, everything was deemed necessary. The specimens were processed at the Army Medical Museum by the technical and professional staff on duty there and a final report and diagnosis was given to the donor. At the request of the donor, photographs, as well as slides, were furnished. In this way, it was planned gradually to build up a Museum of Pathology where every specimen would be available to every member of the Academy. It was hoped that eventually the collection could be made available "to every reputable physician, both in Washington and outside as the material could be sent by mail."

The Museum of Ophthalmic Pathology almost immediately got off to a good start when Dr. James Moore Ball of St. Louis contributed his entire ophthalmic museum and pathology collection to the Army Medical Museum on July 4, 1922 (fig. 20) (Coupal, J. F., 1923). Thereafter, things progressed more slowly and we find Dr. Gradle in his 1924 report complaining that there had not been the response from the membership of the Academy and the profession at large which had been anticipated. By 1927, however, Gradle was becoming more optimistic and he reported that the Committee on Ophthalmic Pathology, working in conjunction with the Academy was continuing the growth of its work. Ophthalmic specimens were being sent in to the Army Medical Museum in greater numbers and there were then about 2,000 specimens contributed mainly by members of the Acadmy. This increased growth, however, presented a new problem, for the limited facilities and personnel afforded the Museum by Congress was not adequate to keep pace. Gradle stated:

> As a result it becomes absolutely essential that help from this Society be now forthcoming. Why is this help necessary? Because the Museum is just beginning to be in a position to accomplish what they wish to do. One of the great aims of the Museum is not only to be a true pathologic Museum but also to put out study sets. Sets of 50 or 100 slides representing various conditions of ophthalmic pathology, these sets to be loaned to members of the Academy at no cost beyond transportation, for a period not to exceed 3 months. Each slide is accompanied by a complete description and a man desiring to improve his knowledge of pathology can borrow one of these sets from the Museum and, in addition, receive any other information the Museum has, on request.

ST. LOUIS POST-DISPATCH

ST. LOUIS, FRIDAY, MARCH 1, 1929.

DR. J. M. BALL, NOTED OCULIST AND WRITER, DIES

His Work on "Modern Ophthalmology One of Foremost Studies of Eye Diseases Used Today.

Funeral services Monday.

By his own wish, Dr. Ball's body will be cremated and the ashes placed in the Army Medical Museum in Washington, to which in 1922 he donated his collection of anatomical specimens and drawings, charts and casts. The collection, made over a period of 30 years, is said to be second only to that of Dr. George E. de Schweinitz of Philadelphia.

Funeral services will be held at the family residence Monday.

Besides his work on ophthalmology, Dr. Ball wrote two other volumes. "Andreas Vesalius, Reformer of Anatomy," issued in 1916, and "The Back-'Em-Up Men," an account of the days when graveyards were looted for human dissection specimens. The latter book was issued last year.

Fig. 20 (Zimmerman). (Top) Urn containing the ashes of Dr. James Moore Ball, who helped establish the central Museum of Ophthalmic Pathology by contributing his large collection of mounted specimens in 1922. (Neg. No. 60-5500.) (Bottom) Portion of Dr. Ball's obituary in the *St. Louis Post-Dispatch*. (Neg. No. 60-5501.)

In a letter dated March 7, 1926, Gradle wrote to Dr. E. C. Ellett who was then President of the American Academy of Ophthal-

mology and Otolaryngology, strongly recommending that the ophthalmic pathology work being conducted at the Army Medical Museum be subsidized by the various sponsoring societies. He suggested that the Academy appropriate $1,100.00 a year, the American Ophthalmologic Society $300.00 a year, and the Section on Ophthalmology of the American Medical Association $100.00 a year. However, in his official report to the Academy, Gradle suggested that since the Academy's Section on Instruction was expected to show a profit of $1,000.00 for the year, that $500.00 of this could well be given to the Army Medical Museum. Thus began an annual appropriation of $500.00 per year, which continued for several years, mainly to subsidize the preparation of loan sets.

With respect to the annual contribution of $500.00 which the Academy was making in those days, it is interesting to note that Dr. Gradle began his report at the 1934 meeting as follows:

> Mr. Chairman and Members: I should like to tell you what you are getting for your $500. In the first place the Academy is no longer bearing the entire brunt of the work on ophthalmic pathology. By changing the name very slightly we have been able to enlist the aid of the National Research Council, so now we are known as the Division of Ophthalmic Pathology of the American Registry of Pathology.

The first description of the then newly organized American Registry of Pathology to appear in the *Transactions* of the American Academy of Ophthalmology and Otolaryngology was contained in Callender's 1930 report, by which time there were, in addition to the Ophthalmic Pathology Registry sponsored by the Academy, the Lymphatic Tumor Registry sponsored by the American Association of Pathologists and Bacteriologists in 1925, and the Bladder Tumor Registry sponsored by the American Urological Association in 1927. In order that adequate support might be obtained and a continuous policy be carried out, Dr. Ludwig Hektoen, chairman of the Division of Medical Sciences of the National Research Council, appointed a Committee for the American Registry of Pathology which was approved by the National Research Council on June 12, 1930. It was composed of the following distinguished persons: Dr. Howard T. Karsner, chairman, Dr. Bowman C. Crowell, Dr. James Ewing, Dr. Harry S. Gradle, Dr. Herman L. Kretschmer, Dr. Stanley P. Reimann, and Dr. George R. Callender, secretary. Callender appended to his report a detailed outline of the object and scope of the American Registry of Pathology. The Registry plan was approved by the American Association of Pathologists and Bacteriologists and by the American Academy of Ophthalmology and Otolaryngology at their respective meetings in 1930.

At this point, it is well for us to recall that while we, today, take for granted our registries as an essential part of modern medicine, back in 1922, when the Academy and the Museum first established the collaborative effort which we now call the Registry of Ophthalmic Pathology, the Registry concept was brand new. The first of all the national registries, the Bone Sarcoma Registry, is only slightly older than ours. The Bone Sarcoma Registry was started by Dr. E. A. Codman for and by the family of a patient whom he had under his care for a supposed bone sarcoma (fig. 21). Codman and the patient's family wished to ascertain the actual facts as to whether there were any living patients who were cured of this disease, and if there actually were, to ascertain the methods of treatment by which these patients had been saved. The family gave one thousand dollars to pay expenses in obtaining the required facts. Codman solicited the advice of Ewing and Bloodgood and established a collection of cases. Through the kindness of personal friends in several clinics, Codman began follow-up investigation. The monetary gift stimulated Codman and many others to work even more vigorously and soon led the Regents of the American College of Surgeons to add an aggregate of $8,000.00 more, contributed from time to time, in order to an-

swer these two simple questions. (See Codman references.)

It soon appeared that by-products were to be the result of this work rather than the intended products of obtaining the answers to the original two questions. The Registry itself was a by-product, for when the original collection of cases could no longer be of possible benefit to the original patient (who by that time had died), the Regents saw that the same questions would be eternal. The friends of future patients would always want to know of the living patients and how they were cured. It is interesting to note that Codman lists among the many by-products of the Registry of Bone Sarcomas during its first five years of existence, "the founding of other registries." I feel certain that Codman must have had the Registry of Ophthalmic Pathology at the Army Medical Museum in mind when this was published in 1926.

The registration date of the first cases placed in the Bone Sarcoma Registry, is July 17, 1920. It was less than one year later that the representatives of the American Academy of Ophthalmology and Otolaryngology and of the Army Medical Museum met to make plans for a central laboratory for ophthalmic pathology at the Army Medical Museum.

During the first decade of its existence, the Registry of Ophthalmic Pathology already began to demonstrate its potential along the three main functional lines which characterize the entire program of the Armed Forces Institute of Pathology today, namely, consultative service, education, and research. Diagnostic service was most important during the early days because at that time there were only three or four American laboratories for ophthalmic pathology in active operation, and the total number of specimens examined each year was about 300 (Friedenwald, 1949). When the American Ophthalmological Society and the Section on Ophthalmology of the American Medical Association joined the Academy in promoting the ophthalmic pathology laboratory at the Army Medical Museum in 1923, the nation's ophthalmologists were repeatedly urged to send their specimens to the Museum along with the always-important clinical histories. As a result, the more than 50,000 cases now on file in the Registry of Ophthalmic Pathology provide much valuable material for education and research.

The diagnostic and consultative service which the Museum has provided civilian ophthalmologists over the years has not been confined to the field of pathologic anatomy, as the following interesting exchange of correspondence attests. In February 1934, Major V. H. Cornell (fig. 22), then the Curator of the Museum, learned through Dr. John N. Evans of Brooklyn that an original Helmholtz ophthalmoscope had just been presented to a Boston hospital by Dr. David Harrower of Worcester, Massachusetts. Major Cornell wrote to Dr. Harrower, advising him of the unexcelled collection of ophthalmoscopes in the Museum and invited him to contribute the original Helmholtz instrument, since the Museum contained only an "excellent copy" of the original Helmholtz.

Dr. Harrower replied on February 28, 1934 as follows:

> The Helmholtz ophthalmoscope that you asked about was brought to this country by Dr. Foster Haven, from Europe in 1858. Dr. Haven started the practice of ophthalmology about that time. When the Civil War broke out, Dr. Haven went to the front, where he was killed.
>
> This instrument with a very rare set of trial glasses, and frames, also brought from Europe, came into the possession of Dr. Thomas H. Gage, from whom I received them.
>
> Last year, I presented a small collection of spectacle frames and ophthalmoscopes, to the Howe Laboratory, in the Massachusetts Eye and Ear Infirmary in Boston, in memory of my dearly beloved friend, Dr. George S. Derby.
>
> I think if you would write to Dr. F. H. Verhoeff, who has charge of the collection, he would be glad to have a photograph made for you.
>
> Trusting to have the pleasure of meeting you sometime, I am,
>
> Cordially yours,
> /s/ David Harrower

Dr. Verhoeff advised Major Cornell on March 8, 1934, that he would present the matter of giving the Museum the Helmholtz

REGISTER

NAME	ADDRESS	INTRODUCED BY

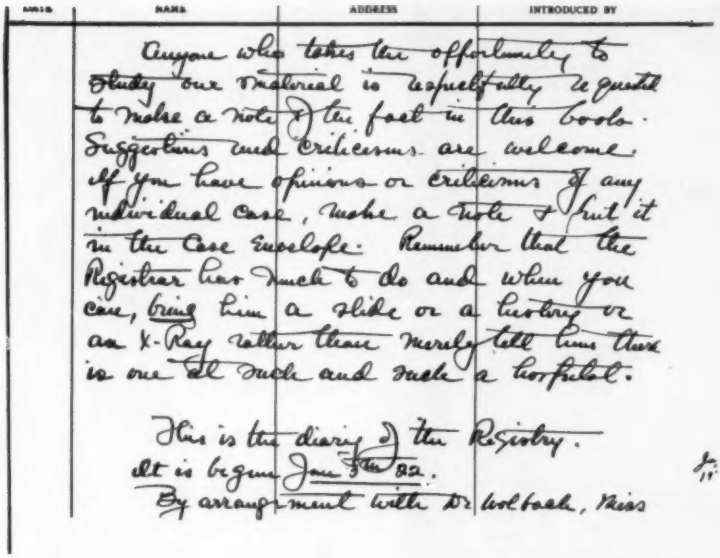
The Registry of Bone Sarcoma.

The primary object of this Registry is to keep an up to date list of all cases of living supposed-to-be-bone sarcoma cases. We register every case:

(1.) of which we have a brief history and an X-Ray picture or a slide or tissue.

(2) certain interesting or unusual bone tumor cases which have been confused with sarcoma.

Up to January first 1920 the expenses of the work were paid by the friends of a patient whom it was supposed probably had a sarcoma of the ilium. Autopsy eventually showed that the disease was malignant cancer. However the material collected for the object of advising treatment in the case of this patient seemed too valuable to lose, and it was realized that it formed a nucleus for a valuable study of this disease, which might be of benefit to future patients. Accordingly the Registry was informally organized by Dr J. C. Bloodgood of Baltimore, Dr James Ewing of New York and Dr E. A. Codman of Boston. At the suggestion of some of the surgeons who had became interested in the work the American College of Surgeons has taken the Registry over as a part of its work and will hereafter pay the incidental expenses necessary.


NAME ADDRESS INTRODUCED BY

Anyone who takes the opportunity to study our material is respectfully requested to make a note of the fact in this book. Suggestions and criticisms are welcome. If you have opinions or criticisms of any individual case, make a note & put it in the case envelope. Remember that the Registrar has much to do and when you can, bring him a slide or a histology or an X-Ray rather than merely tell him that is one of such and such a hospital.

This is the diary of the Registry. It is begun Jan 5th 22.

By arrangement with Dr Wolbach, Miss

Fig. 21 (Zimmerman). Excerpts from the original Register of Dr. E. A. Codman's Bone Sarcoma Registry, written by Dr. Codman.

ophthalmoscope at the next meeting of the Howe Library Committee, though he doubted very much if they would be willing to part with the instrument. However, on June 1, 1934, Dr. Verhoeff advised Major Cornell as follows:

I am sending you the ophthalmoscope that Dr. Harrower presented to the Howe Library Museum, but it certainly is not an original Helmholtz ophthalmoscope, because it has a silvered mirror and the first Helmholtz Ophthalmoscope did not have a silvered mirror. If, after you have examined it, you do not find it of sufficient interest to keep, or if you already have one like it, please return it to us.

The instrument was received at the Museum, examined, and returned to the Massachusetts Eye and Ear Infirmary in June, 1934, with the following report from Major Cornell addressed to Dr. George H. Bigelow, Director of the Infirmary:

Thank you very much for your courtesy in sending us the ophthalmoscope, which was received in good condition.

We are returning it by parcel post insured this date as, after inspecting it, Major Davis, who has made quite a study of these instruments, has decided that it is not a Helmholtz instrument but a Jaeger of which we already have several specimens. I am enclosing a photograph of a Helmholtz instrument of 1851,* of our own Jaeger, 1854 (Acc. No. 22143), and of the instrument presented to your collection by Dr. Harrower. I am also enclosing a list of notes made by Major Davis on which he bases his conclusions that this instrument is a Jaeger. You will note that Dr. Haskett Derby contributed one of the 1854 model Jaeger instruments to the Army Medical Museum in 1901.

I assure you we appreciate very much your kind cooperation but as this is not the instrument that we had hoped it might be, we are returning it to your collection with our sincere thanks.

Thus the Museum, as a result of its long and intense interest in ophthalmoscopes, was in a position to make a positive identification and to squelch the rumor that an original Helmholtz ophthalmoscope was in the possession of the Howe Laboratory of Harvard University.

The Museum became actively interested in the collection and study of ophthalmoscopes, largely under the influence of Dr. Harry Friedenwald of Baltimore who, together with Dr. Casey Wood, formed a committee to arrange exercises and an historic exhibit for

* See Figures 23 and 24.

Fig. 22 (Zimmerman). Col. Virgil Heath Cornell, MC, USA, curator of the Army Medical Museum, 1933-1935. (Neg. No. 57-348.)

the American Medical Association's meeting of 1901, to commemorate the 50th anniversary of the invention of the ophthalmoscope. Before that time the Museum had acquired only six or seven ophthalmoscopes. Drs. Friedenwald and Wood consulted with the Surgeon General of the Army and the Curator of the Museum, as a result of which it was decided that the Museum should ideally house and preserve for posterity the Nation's collection of old ophthalmoscopes. On June 22, 1901, Dr. Harry Friedenwald, in a letter to the Curator, stated that the Section on Ophthalmology of the American Medical Association, at its annual meeting in St. Paul, adopted a resolution to arrange a permanent historical exhibit of ophthalmoscopes at the Museum. All physicians who had loaned ophthalmoscopes for the exhibit at the AMA meeting were invited to contribute their instruments to the Museum. Unfortunately, the response was not as enthusiastic as Drs. Friedenwald and Wood had hoped. Thirty years later, on October 22, 1930, Dr. Harry Friedenwald wrote as follows to Major George R. Callender, who was then Director of the American Registry of Pathology:

> Many years ago, on the occasion of the 50th anniversary of the invention of the ophthalmoscope, I undertook, on behalf of a small committee composed of Dr. Casey A. Wood and myself, to arrange for an exhibition of ophthalmoscopes at the Minneapolis meeting of the A.M.A.
>
> I am sending a brief description of this collection because all remembrances of it has probably been lost, except to those who saw it. I secured a large number of instruments as loans for this exhibition, some of which were quite unique. Thus, for example, a large Ruete ophthalmoscope was exhibited which could not be found in Germany when they arranged a similar exhibition and the committee had to construct one from the original description.
>
> At the close of the exhibition, I took the matter up with your Museum and suggested that an en-

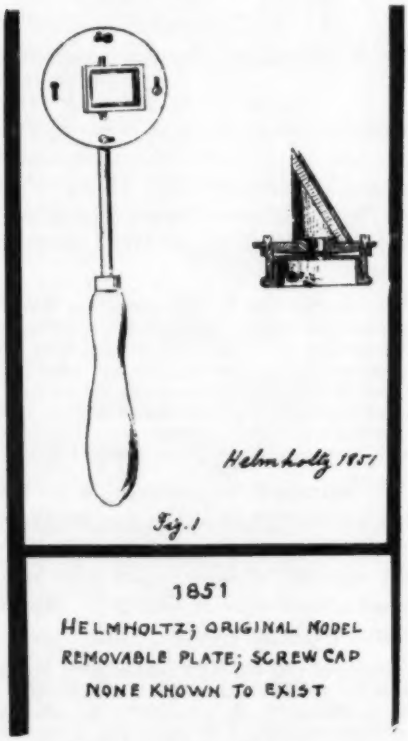


Fig. 23 (Zimmerman). Sketch of original Helmholtz ophthalmoscope from old ophthalmoscope exhibit of Army Medical Museum. (Neg. No. 33533-2.)

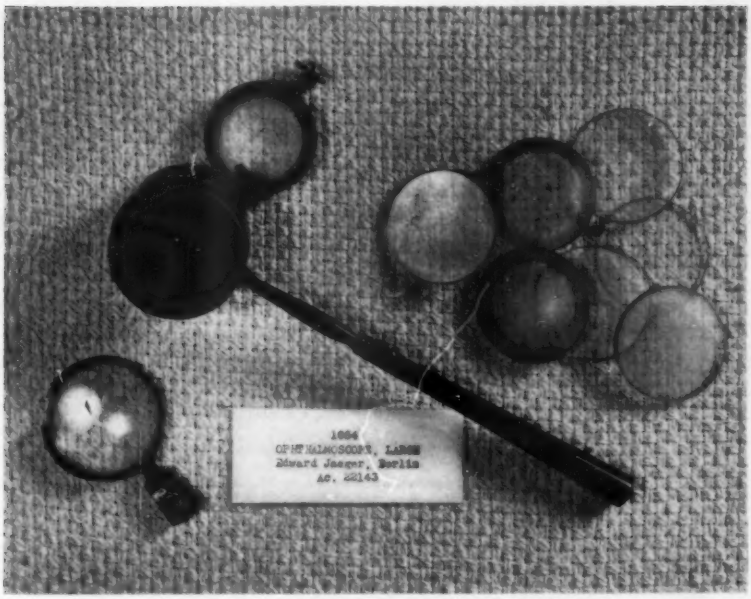


Fig. 24 (Zimmerman). Jaeger ophthalmoscope (1854) from Army Medical Museum's collection. (AFIP Acc. No. 22143.)

deavor be made to obtain as many of these instruments as gifts or permanent loans for your Museum, and I wrote requests to those who had been kind enough to loan their instruments for the Minneapolis exhibition asking them to give or loan them to the Army Medical Museum. I remember that a number of valuable instruments were promised in this way.

On visiting the Museum, I was able to find but a very few and I am writing to ask whether an effort could not be made to have an adequate exhibition in the Army Medical Museum. I believe that even now, some of these instruments that were described could be obtained, and certainly others. With the passage of time, it will become more and more difficult to secure these instruments. I should like to know what your views are on the subject.

With kindest regards, I am,

Very truly yours,
/s/ Harry Friedenwald

Major Callender replied to Dr. Friedenwald that the collection of ophthalmoscopes had not been forgotten and that the entire collection was being "worked-up" with a view to its exhibition in one place, as it had not been exhibited since 1922.

Dr. Friedenwald's suggestion was followed and an effort was made to contact the descendents of those deceased who owned instruments at the time of the 1901 AMA meeting, but, unfortunately, in every case, no trace of such instruments could be found. In 1930 the collection was relabeled and placed on full exhibit at the Museum.

The Museum presently has a large descriptive catalogue of its ophthalmoscope collection. This catalogue was prepared in 1944 by Major Harry A. Davis, U. S. Army Retired. Major Davis was then in charge of the Historical Section of the Museum and is the person who identified as a Jaeger the alleged original Helmholtz instrument given to the Howe Laboratory by Dr. Harrower. On March 14, 1950, Dr. Harry Friedenwald presented his own Helmholtz ophthalmoscope as a permanent gift to the Army Medical Museum. This acquisition is of especial historical significance because it was made especially for Prof. Albrecht von Graefe, who ordered it the year Helmholtz described his invention (figs. 25-29).

Colonel Albert E. Minns, Jr., the present Curator of the Museum of the Armed Forces

Institute of Pathology, has asked me to call to your attention that the Medical Museum is still very much interested in acquiring ophthalmic and otolaryngic instruments of all types. Any of you who are in the possession of old surgical instruments which you would like to donate to the Museum's historical collection should contact Colonel Minns at the Museum, or you certainly may write to me.

Educational activities

1. On-the-job training

When the Army Medical Museum first began its concerted efforts to provide diagnostic service in ophthalmic pathology, the staff pathologists and technicians had to be trained for this new work. Initially most of this training was provided by Dr. Verhoeff, and later by Drs. Friedenwald and Theobald. Major Callender, some of his successors in the position of Curator of the Museum, and other members of the staff ultimately became extremely competent ophthalmic pathologists by virtue of their opportunity to study the collected cases in the Registry and to learn from their predecessors. Besides Callender,

In Reply Refer to S.G.O. .....

WAR DEPARTMENT.
OFFICE OF THE SURGEON GENERAL,
ARMY MEDICAL MUSEUM AND LIBRARY,
WASHINGTON.

22 Apr. 1939

Dr. Harry Friedenwald
1212 Eutaw Place
Baltimore, Md.

Dear Dr. Friedenwald:-

The Helmholtz instrument we have was purchased in 1902 from J.Odelga, Vienna. It was listed in his catalog of 1887, and the purchase order specifically stated it MUST be exactly like the one listed in the cat. of 1887. This instrument differs from the original in that the PLATE is fixed and not removable, the original had a plate with 4 screws and was removable, the cap is a friction one while in the original cut of Helmholtz monograph the description states "eingeschraubt ist", screwed in. The cut also shows screw action. Photograph of this cut on exhibit.

Concerning the [illegible] shown at the meeting of 1902,correspondence was had with the owners of many of the instruments which resulted in some being donated and one or two were purchased. Of the five listed as Helmholtz none was obtained. The pictures of these instruments all show the PLATES are fixed and no evidence of being removable all probably had friction caps. I tried about 1929 to locate some of them but no trace could be found of Harlan and Chisholm, Dr. Thomson, or Jeffries. That of Dr.Young he stated he had given it to North Western University.

I was particularly anxious to secure that of Dr. Thomson as it had belonged to Brinton who was an early Curator of this Museum.

The Library has copies of Hemlholtz publications, any way thanks for your offer to inspect your copy.

I have tried several places to have a copy of the original Helmholtz duplicated but the cost is almost prohibitive. If we ever get flush with funds I intend to have a copy made.

If you ever part with your instrument do not forget this collection as it would form a valuable part of it.

Very truly,

Harry A. Davis
Maj. USA Ret.
Hist. Section.

Fig. 25 (Zimmerman). Major Harry A. Davis' letter of April 22, 1939, inviting Dr. Harry Friedenwald to contribute his Helmholtz ophthalmoscope to the Museum's collection (see fig. 29.) (Neg. No. 60-5501-4.)

DR. JONAS S. FRIEDENWALD
DR. ERNST BODENHEIMER
1818 EUTAW PLACE
BALTIMORE-17 MD.

March 14, 1950.

Dr. Ruell A. Sloan, Curator,
Medical Museum,
Washington, D. C.

Dear Doctor Sloan:

Replying to your very kind letter of February 20th, I desire to express my great satisfaction with the complimentary note of the services I have given to the Museum.

I have definitely determined to present my Helmholz Ophthalmoscope as a permanent gift to the Museum. In this my son, Dr. Jonas S. Friedenwald, joins heartily.

There are certain features of the gift which require special mention. The instrument was made by E. Sydow, an able optical mechanic of Berlin. It was made by the order of Professor Albrecht von Graefe in the first year in which Helmholz described his invention, and von Graefe used this very instrument during his all too few years of medical practice. These facts were communicated to me by Mr. Sydow who regained possession of the instrument after von Graefe's death. In 1888 I obtained the instrument from Mr. Sydow, at which time I was serving as first assistant in the Eye Clinic of Professor Julius Hirschberg.

I confess that the possession and use of this instrument by Professor von Graefe has ever made it more precious to me.

I am also sending the earliest description of his "Augenspiel" if you will accept it as a companion piece to the ophthalmoscope.

I am not familiar with the regulations of the Museum. You will therefore permit me to state that I should not insist upon the instrument being withheld from any loan for exhibit purposes, provided adequate safeguards against its possible injury or loss are assured.

Awaiting your reply and a safe coupling to Washington, I am

Very truly yours,

Harry Friedenwald

Fig. 26 (Zimmerman). Dr. Harry Friedenwald's letter of March 14, 1950, advising the curator of the Army Medical Museum of his decision to place his Helmholtz ophthalmoscope in the Museum's collection. (Neg. No. 60-5501-5.)

James E. ("Dee-Dee") Ash (fig. 30), Elbert ("Frenchy") DeCoursey (fig. 31), and Helenor Campbell ("Hellie") Wilder (fig. 32) became especially well known because of their interest in ophthalmic pathology. As Callender pointed out at the Academy meeting in 1953, Mrs. Wilder, who joined the Museum staff shortly before the establishment of the Ophthalmic Pathology Registry and who became a student of eye pathology with him and his successors at the Museum, is and has been the person to whom the highest credit is due for the operation of the Registry and the success it has achieved. Her outstanding contributions to histopathologic technique; her magnificent exhibits displayed over the years at the annual meetings of the Academy and at other national and in-

ternational meetings of ophthalmologists; her extensive studies of intraocular neoplasms, of ocular injuries sustained by soldiers in World War II, of the ocular pathology observed in atomic bomb casualties; and then shortly before her retirement from the Registry, her demonstration of nematode larvae in pseudoglioma, hitherto blamed on almost everything but parasites, and Toxoplasma in a disease which had for years been called tuberculous, testify not only to her own industry and abililty as an ophthalmic pathologist but also to the value of having a large central Registry of Ophthalmic Pathology.

Another person who has participated in this on-the-job training, initially as a recipient of training in ophthalmic histopathologic technique, and subsequently, over a long period of time which encompasses the entire life of the Registry, as an instructor of technicians who have come to the Museum and to the AFIP for training, is Mr. Lawrence P. Ambrogi, now chief of the Laboratories Branch of the Armed Forces Institute of Pathology. We have been remarkably fortunate that a person of his ability, personality, and interest in ophthalmic pathology has remained in almost continuous employment at the Institute since 1920.* The only interrup-

* On December 17, 1960, while preparing an eye for histopathologic study in the laboratory of the Washington Hospital Center, Mr. Ambrogi was stricken with a massive myocardial infarction, which proved fatal the following day. "Larry" will never be forgotten by his many friends and colleagues, nor will he ever be replaced. It is fortunate, however, that he had always shared his "tricks-of-the-trade" so generously, and that his lovable character and diplomatic nature "rubbed off" on so many of his associates. His influence will be long-lasting.

DR. HARRY FRIEDENWALD
DR. JONAS S. FRIEDENWALD
DR. ERNST BODENHEIMER
1818 EUTAW PLACE

BALTIMORE-17, MD.

May 2, 1 951.

Dr. Ruell A. Sloan
Medical Museum
Armed Forces Institute of Pathology
7th St. & Independence Ave. S.W.
Washington 25, D.C.

Dear Dr. Sloan:

You will remember that a little over a year ago I brought you the Helmholtz ophthalmoscope which my father had purchased in Berlin during his student days there. My father had been assured by the manufacturer that this particular instrument had been originally made for Professor Von Graefe and had been re-purchased from Von Graefe's estate after his death.

My father was quite sure that he had had a certificate from the manufacturer stating the facts about this instrument and I had made an extended search for that certificate before turning the instrument over to you, and was very unhappy at the time not to have been able to find it. Just today, in going over some of my father's papers, I came across the certificate which I am happy to send you enclosed as an addendum to the original gift of the instrument.

With kind regards,

Sincerely yours,

Jonas S. Friedenwald, M.D.

Fig. 27 (Zimmerman). Dr. Jonas S. Friedenwald's letter to the curator on May 2, 1951, announcing the recovery of the document which verified the fact that his father's Helmholtz ophthalmoscope had originally belonged to Prof. Albrecht von Graefe (see fig. 28). (Neg. No. 60-5501-6.)

Fig. 28 (Zimmerman). Letter written June, 1889, to Dr. Harry Friedenwald by Emil Sydow, who constructed the Helmholtz ophthalmoscope for Prof. Albrecht von Graefe, confirming the fact that von Graefe had used the instrument in his practice. (Neg. No. 60-5501-3.)

tions were between 1922 and 1926, part of which time was the two-year period when he accompanied Callender to the Far East.

Thus the Museum (as Gradle predicted) soon became a "Mecca" for training in ophthalmic pathology. Over the years this phase of the educational program based on the Registry material has become increasingly prominent. For several years now, the Academy has sponsored a fellow in ophthalmic pathology at the Armed Forces Institute of Pathology. In addition, many others have come to study the Registry material on funds provided by their respective military services or civilian institutions, by the Heed Ophthalmic Foundation, by the National Institute of Neurological Diseases and Blindness, and by other philanthropic organizations. At the present time there are seven such full-time physicians in training and almost as many part-time trainees in the Ophthalmic Pathology Branch of the Armed Forces Institute of Pathology. Similar on-the-job training is given to histopathology technicians sent to

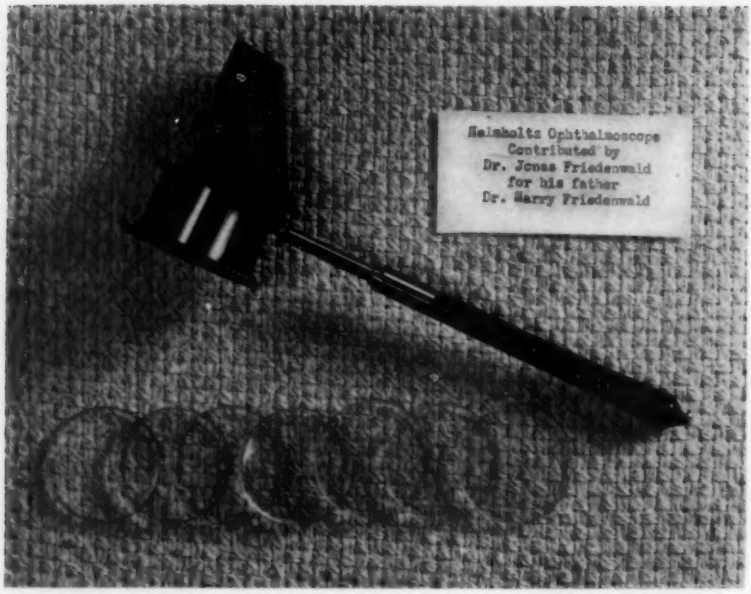


Fig. 29 (Zimmerman). Prof. Albrecht von Graefe's Helmholtz ophthalmoscope obtained by Dr. Harry Friedenwald in 1888 (see figs. 26-28). (AFIP Acc. No. 295211.)

the Armed Forces Institute of Pathology by their respective institutions to learn the methods used to prepare and stain celloidin and paraffin sections for light microscopy and ultrathin methacrylate sections for electron microscopy of the eye.

2. Instruction by reports

From the standpoint of individual instruction, one of the least appreciated but probably one of the most significant contributions of the Registry program throughout the years has been the subtle yet profound effect of providing a detailed gross description and histopathologic report together with representative microslides to the pathologist and/or ophthalmologist who contributed each specimen to the Registry. In the early days, these reports often had extensive direct quotes from such leading authorities as Dr. Verhoeff, and even today in controversial situations the opinions of several experts may be obtained and forwarded to the contributor along with the opinions of the Registry staff. By reviewing the microslides along with the written reports, many ophthalmologists have, over an extended period of time, been better able to keep up in the field of ophthalmic pathology, even though they might be located in a rural area far away from any large medical center. In certain larger cities where residency training programs in ophthalmology are in effect, these reports and microslides are used for group instruction. I should like to re-emphasize that, in my opinion, this extremely subtle and unpublicized educational activity of the Registry is the one which probably has the greatest practical influence on the contributors to the Registry.

3. Preparation of exhibits

It is historically significant that in the initial proposal to establish a Museum of Ophthalmic and Oto-laryngologic Pathology at the Army Medical Museum, Dr. Gradle outlined to the Academy his plans, which included the hope that not only would interesting and instructive cases be exhibited at the

Museum but also that the Museum would have at the annual meeting of the Academy, an exhibit of interesting cases sent in during the year (fig. 16, Gradle, 1921). Such an exhibit was prepared for the 1922 Academy meeting though, judging from Gradle's letter to Surgeon General Ireland (already quoted) and from some of his initial annual reports, these first few exhibits must not have met his expectations. At the 1924 meeting he complained that the Academy membership was not supporting the program to the extent which it should and, as a result of this, "the display we have set up this year is somewhat limited." Later, however, Gradle's dreams came true and a series of fine exhibits based on the Registry collection was prepared for the Academy and for other important meetings (fig. 33). By 1928, exhibits had been sent to meetings in Minneapolis, Montreal, Detroit, Boston, London,

Fig. 30 (Zimmerman). Colonel James Earle Ash, MC, USA, who during his two tours as curator of the Army Medical Museum and director of the Army Institute of Pathology guided the organization for a longer period than any other person since the Army Medical Museum's second curator, Lieut. Colonel Surgeon George Alexander Otis, who spent 18 years as curator. During Colonel Ash's second tour the Registry program experienced its greatest growth and the Museum blossomed into the Army Institute of Pathology. (Neg. No. 81108.)

Fig. 31 (Zimmerman). Brig. General Elbert DeCoursey, MC, USA, who as a young pathologist assigned to the Army Medical Museum became much interested in ocular pathology and prepared the first three editions of the old *Atlas* in collaboration with Ash, Wilder, Ambrogi and Reeves. Later General DeCoursey became the first director of the AFIP in its new building at Walter Reed Army Medical Center. (Neg. No. 55-14699.)

Fig. 32 (Zimmerman). Dr. Hans F. Smetana presenting Mrs. Helenor Campbell Foerster (the former Helenor C. Wilder) with a gift from her friends and colleagues at the time of her retirement from the Armed Forces Institute of Pathology. Others in the picture are Mrs. James E. Ash and General DeCoursey. (Neg. No. 53-9249-2.)

and Colorado Springs. Some of the more outstanding exhibits of recent years have covered such subjects as comparative anatomy of the eye (1941), conditions of unusual interest in the Registry of Ophthalmic Pathology (1943), injuries of the eye (1944), malignant melanoma of the uveal tract (1949), organisms identified in inflammatory lesions in the eye (1953), pathologic diagnosis of granulomatous inflammations of the eye (1954), pathology of the optic nerve (1955), processing of the whole eye in paraffin (1958), and clinicopathologic study of the cornea (1959).

4. Loan sets

In his 1926 report, Gradle indicated that "eventually the Museum will prepare study sets of 100 or 200 characteristic specimens, that will be loaned to men throughout the country for a period of three or four months as they desire in order that men may carry on their pathologic studies at home without having to leave their work." Preparation of these loan sets was a costly affair that required annual subsidization by the Academy. However, in the two decades that followed, several large and quite complete loan sets were prepared and these have proved to be of very great value, particularly to those individuals who once or twice each year find it necessary to make an intensive review of ophthalmic pathology prior to writing the American Board Examinations. These study sets are also used in formal courses offered at the Armed Forces Institute of Pathology as well as in universities where similar sets are not available. By 1930 Callender was able to report that in the course of the previous five years, 12 sets of 100 slides each had been prepared under the auspices of the American Academy of Ophthalmology and

Otolaryngology and concluded, "Thus the use of the collection as an educational measure has been included in the activities of the department."

5. Atlases

The first extensive use that was made of the Registry Collection for illustrative purposes was in Dr. Jonas S. Friedenwald's book on *The Pathology of the Eye,* published by the Macmillan Company in 1929. This book was extensively illustrated with 253 photomicrographs from the collections of the Wilmer Ophthalmological Institute and from the Army Medical Museum. Most of these illustrations were prepared by Miss Helenor Campbell (who later became the famous Mrs. Wilder).

The first real *Atlas of Ophthalmic Pathology* and its companion in *Otolaryngic Pathology* were the outgrowth of the syllabuses which were prepared to accompany the loan sets of slides. It was felt that the *Atlases,* because of their greater convenience, would have broader appeal to busy clinicians who desired to review the pathology of their specialties. In addition, they made it possible to cover the fields more comprehensively, as there was not the limitation in selection of cases through scarcity of material for slides that restricted the scope of loan sets. At the instigation of Dr. Ralph A. Fenton in 1937, the Academy sponsored the publication of the *Atlases* as part of its educational activity. The first edition of the *Atlas of Ophthalmic Pathology* appeared in 1938 under the joint authorship of Capt. Elbert DeCoursey, pathologist to the Registry, and Lieut. Col. James E. Ash, curator of the Army Medical Museum, with credits to Mrs. Helenor C. Wilder, microscopist, Mr. Roy M. Reeve, photographer, and Mr. Lawrence P. Ambrogi, technician.

The *Atlas of Ophthalmic Pathology* immediately received an enthusiastic response, and on December 10, 1938, Col. Ash wrote to Dr. Gradle that the first printing of the *Atlases* was already exhausted and "we are about half way through the second." The second edition of this book, which came out the following year, and a third edition prepared in 1942 were products of the same collaboration.

Then, following the end of World War II, it was felt that there was a need for combining the *Atlas* with additional textual material that would cover not only the fundamentals in descriptive pathologic anatomy of the eye but also certain basic principles of pathology (Benedict, et al., 1953). Thus the

Fig. 33 (Zimmerman). At the 1947 Academy meeting, Colonel Ash demonstrated temporal bone pathology of aviators, while Mrs. Wilder described the ocular pathology found in atomic bomb casualties. (Neg. No. 547-B.)

Academy and the Institute of Pathology (then named the Army Institute of Pathology) again joined forces to establish a committee under the guidance of Dr. Brittain F. Payne which would undertake the preparation of a new *Atlas and Textbook on Ophthalmic Pathology*. After many years of hard work, the first edition of this book was published in 1952 with Dr. Jonas S. Friedenwald serving as editor-in-chief. Several years ago, a new committee of authors headed by Dr. Michael J. Hogan was established by the Academy and the Armed Forces Institute of Pathology to prepare a second edition of this *Atlas and Textbook*, which will be available within a few months.

6. Formal courses

Beginning in about 1937, the Registry staff began to participate in formal teaching programs. For many years the staff was responsible for the pathology portion of the postgraduate course in ophthalmology given by the George Washington University (fig. 34). After World War II, with the great increased demand for instruction in all aspects of medicine and pathology, the number of formal courses in which the Registry staff participated greatly increased. These included, in addition to such well-established endeavors as Dr. Georgiana Theobald's annual course in ophthalmic pathology presented at the time of the annual meeting of the Academy and Dr. Parker Heath's two weeks of ophthalmic pathology during the Lancaster courses in ophthalmology offered each summer, short special courses offered at the Institute. The annual course in ophthalmic pathology conducted at the Armed Forces Institute of Pathology has become increasingly popular so that it has become necessary to turn away each year many who cannot be accommodated by the limited facilities available. Thus another of Gradle's great visions, which he was so timid about expressing in his letter to Walter R. Parker on August 26, 1922 (previously quoted), has come true. The Registry staff has also played host to the Ophthalmic Pathology Club at each of its annual meetings since

Fig. 34 (Zimmerman). One of a series of postgraduate classes in ophthalmic pathology sponsored by George Washington University at the Army Medical Museum. Colonel Ash and Mrs. Wilder are standing among the students. (Neg. No. 540-2.)

1947, except for the one held at Wills Eye Hospital in Philadelphia in 1954 (fig. 35).

Research activities

While Dr. Harry Gradle seems to have been the person most interested in and responsible for developing a center of ophthalmic pathology, he was principally concerned with the need for furnishing diagnostic service and for providing postgraduate education. I believe that Dr. George R. Callender deserves the credit for calling attention to the fact that this ophthalmic pathology collection and the Registry into which it evolved would provide a wealth of material for important research.

Perusal of the first several annual reports prepared mainly by Dr. Gradle reveals little if any evidence that the collection eventually might be used for research. However, in 1928, Callender and Campbell revealed that a questionnaire (history form) had been prepared under the direction of the committee representing the American Academy of Ophthalmology and Otolaryngology, the American Ophthalmological Society, the Section on Ophthalmology of the American Medical Association, and the Army Medical Museum. It was hoped that the co-operation of the contributors in providing the clinical data requested by the questionnaire and in following up their cases would result in the accumulation of much interesting and valuable information. Then, in 1930, after the American Registry of Pathology had been formally established and the Section and Museum of Ophthalmic Pathology had provided the material for the first of the constituent registries, that is, the Registry of Ophthalmic Pathology, Callender outlined the objective of the Registry program and indicated how this national collection might be used for research purposes. He pointed out that except at the large medical centers, too few cases of any one kind can be accumulated to obtain results on which reasonable clinical judgments can be based. By combining the cases accumulated by the centers with the cases of the American Registry of Pathology obtained from the country as a whole, it would be possible to obtain considerable numbers in a much shorter time. It was the purpose of the Registry, therefore, to cooperate to the fullest extent with all such groups to the end that uniform nomenclature might be used and that the greatest amount of knowledge might be obtained in the shortest time. He pointed out that the value of such investigations had been repeatedly demonstrated, but never better than

Fig. 35 (Zimmerman). First annual meeting of the Ophthalmic Pathology Club, April, 1947. Of the 14 meetings held to date, 13 have been at the AFIP. (Neg. No. 517-2.)

by the Registry of Bone Tumors of the American College of Surgeons (see Codman's reports of 1922-1926). He stated that by means of the study of these cases many lives had been saved and many deforming operations had been avoided. The Registry had made significant advances in the knowledge of the criteria for diagnosis, the outcome, course and methods and treatment of bone tumors, and was still adding to the accumulated knowledge of these tumors.

Thus the Registry of Ophthalmic Pathology would be used for research in a manner comparable to that which had proved so fruitful in the field of bone tumor pathology. The following year, Callender showed that this was not merely a dream but that actual results had already been obtained. It was at the Academy meeting of 1931 that Callender described his histopathologic classification of malignant melanomas of the uvea (which was based on 111 cases) and called attention to the diagnostic significance of his classification. As no precedent was found for this method of classification of malignant melanotic tumors of the eye in a search through the *Index Catalogue* of the Army Medical Library, no bibliography was appended.

In opening the discussion of Major Callender's historical paper, Dr. Jonas S. Friedenwald stated:

> We are all deeply indebted to Major Callender, not only for his beautifully clear presentation of this important study, but also for the interest and tireless diligence which he has for so long given to the ophthalmic collections of the Army Medical Museum. Our Society has a very special interest in this work. The Section on Ophthalmology of the American Medical Association and the American Ophthalmological Society joined with us in 1923 to establish a special ophthalmic division in this national Registry of Pathology, thus enabling physicians all over the country to send specimens and get well considered pathological diagnoses. But the contributions of the other Societies have been mainly spiritual, while that of this Academy has been the material essence, without which the division would not have functioned. It is very fitting that the first important statistical study to emanate from this collection should be presented before this Society.

Recently, in talking with Dr. Callender, I found him to be extremely modest and unwilling to speak about many of his historically significant contributions in getting the Registry program started, but I did learn that he was extremely pleased that his original classification of the uveal melanomas had stood the test of time and that the very much larger data that we now have only substantiate the observations which he reported in his initial paper of 1931.

In his annual report of 1931, Callender also summarized the data which had been accumulated from the 45 cases of retinoblastoma received up to that time. It is of interest to note that in that initial series, the incidence of bilaterality (approximately 25 percent) was essentially the same as it is today but the number of cases in which involvement of the optic nerve and extraocular extension had occurred was very much larger than in a comparable series of today. In that initial series of 45 cases, there were 13 in which the nerve was involved and 17 additional cases in which there was extension outside the globe. As Reese has pointed out in his book on *Tumors of the Eye*, the less extensive involvement of retinoblastomas seen nowadays is a tribute to the progress that has been made by ophthalmologists in a relatively short span of time. The advances which have been made in educating parents, pediatricians, and ophthalmologists are responsible for the better prognosis afforded the unfortunate child who is born with retinoblastoma today. Significantly, Callender called attention to the fact that in that first series of 45 cases there were no deaths from the tumor when it had not extended beyond the limits of the globe itself.

The final paragraph of Callender's 1931 annual report to the Academy is of interest:

> The undersigned has not been informed officially of any action taken by the Council with reference to the American Registry of Pathology for the purpose of financing a continuation of this work. The table above indicates rather marked increase in the work and the necessities for such action. It is recommended that the council of the American Academy of Ophthalmology and Otolaryngology give official approval to this effort and take what-

ever means may be at their disposal to assist in obtaining funds to place the whole project on a sound, permanent, financial basis.

/s/ George R. Callender,
Registrar

For a number of years thereafter, the annual report provided much statistical information concerning special studies, particularly those based on the collection of uveal melanomas and retinoblastomas. One of the most complete reports of that type was included in Cornell's report of 1936. By that time, 54 cases of melanoma of the choroid had been followed five years or longer, Mrs. Wilder had developed her improved technique for silver impregnation of reticulum fibers, and Callender and Wilder showed that the more heavily fibered tumors had a much better prognosis than those tumors in which there were few reticulum fibers. Thus, in addition to cytologic classification, the pathologist had an additional histopathologic method of estimating prognosis.

The continued interests of the Army Medical Museum in the affairs of the American Academy of Ophthalmology and Otolaryngology provoked the following letter of appreciation addressed to Maj. Gen. Charles R. Reynolds, who was then Surgeon General of the Army, written by Dr. Ralph A. Fenton, a member of the Board of Trustees of the American Medical Association and an officer of the Academy on October 9, 1936, following the 1936 meeting:

My Dear General, The Council and Membership of the American Academy of Ophthalmology and Otolaryngology are very much pleased with the fine cooperation of Major Cornell and his staff in carrying on work in the pathology of these branches. His exhibit was greatly admired at our meeting in New York last week. Incidentally, Professor Larsell and I have again this year sent in our exhibit of Academy-Financed Research on the Sinuses (lymphatics and innervation) for inclusion in the permanent collections of the Army Medical Museum, and we are getting together a complete file of microscopic slides on our past five years' research to add to the pathologic collection, as requested last year by Major Dart.

The research potential of a large central tumor registry was obvious after the early reports of Callender (1931), Callender and Wilder (1935), and Cornell (1936). Drs. Jonas Friedenwald and Conrad Berens were so stimulated that they influenced the directors of most of the country's leading Ophthalmic Pathology Laboratories to contribute their tumor cases to the Registry. Funds were provided by the Association for Research in Ophthalmology to expedite collection of the cases. As a result of this intensive nation-wide co-operative effort,* the melanoma collection grew rapidly from 273 to 1,238 cases and made possible the very important report by Wilder and Callender in 1939.

Since these studies of intraocular neoplasms are of such historical importance to the Registry, I would now like to show you that these famous collections are still under investigation and that during the past several years they have provided data which have helped answer a number of important questions.

In 1954, for example, Dr. Maumenee stimulated one of his former residents, Dr. Milton Flocks, to see if there was any relationship between the size of a choroidal melanoma and its tendency to metastasize. This was not merely an academic question but one of considerable clinical importance. Difficulties in differential diagnosis are much greater and more frequent with small lesions, and all too often eyes are enucleated because of the possibility that the lesion in question might be malignant. How much danger would there be if instead of performing an enucleation immediately, the patient were followed to determine whether the lesion was growing? Flocks' study led to the demonstration that there is a direct correlation between size of choroidal melanomas and their prognosis, small tumors having a

* The principal contributors were W. L. Benedict, A. B. Cushman, P. DeLong, R. Dominguez, B. Fralick, J. S. Friedenwald, W. E. Fry, S. R. Gifford, B. Klien, A. Knapp, H. D. Lamb, W. F. Moncrieff, C. S. O'Brien, L. T. Post, A. B. Reese, B. Samuels, T. L. Terry, G. D. Theobald, J. A. de Veer, and C. V. Weller.

much better prognosis than large tumors. Furthermore it was found that the probable reason for this difference was the associated difference in cell type found in the two groups. Small tumors are usually composed entirely of the more benign spindle cells, while most of the large tumors contain significant numbers of epithelioid cells (Flocks, Gerende, and Zimmerman, 1955).

A few years later, Makley and Teed were interested in determining the frequency with which malignant melanomas were found in enucleated eyes when the possibility of an intraocular neoplasm had not been suspected clinically. In analyzing 1,000 consecutive cases in the Registry, these investigators found that in 113 (11.3 per cent) the tumor had not been suspected. Most of these eyes had opaque media which prevented visualization of the fundus and they were enucleated because they were "blind and painful." Makley and Teed then asked themselves the question, "What is the danger of not enucleating a blind eye with opaque media?" They found that in almost four percent of adult Caucasian eyes that were blind for at least six months prior to enucleation and in which the fundus could not be visualized because of opaque media, malignant melanomas were present.

It had long been suspected that melanomas of the iris were less malignant than were those of the posterior uvea, but since these tumors are so much less common it took longer to accumulate sufficient data to provide the evidence. In 1958 Rones and I showed that about one half of all iris melanomas in the Registry collection were resectable by iridectomy and that this conservative procedure would suffice. The life span of our patients was not affected by this type of tumor.

Now I would like to give you some of the most recently compiled data based on the Registry collection of malignant melanomas of the choroid and ciliary body. I am indebted to Mr. B. L. Parnell, in particular, for these data because he had to spend such long hours at night and on week-ends to make it possible for me to present these tables and graphs to you. These data are based on 1,872 cases in which the interval between enucleation and last follow-up has been five years or longer. Those cases received in the Registry since the end of 1955 are not included. Patients who died of other causes and those who were "lost-to-follow-up" are also not included in these data. In earlier studies, we had found that the prognosis of patients with "spindle B" and "fascicular" tumors is very similar. Therefore, in the present study, these two groups have been lumped together. For the same reason, the "mixed cell type" and "necrotic" categories have been grouped together.

From the data in Table 2 and the actuarial curves shown in Figure 36, we can make some interesting observations and speculations. Most obvious, of course, is the great difference between the curves for spindle A, spindle B, and fascicular on the one hand, and epithelioid, mixed, and necrotic, on the other. The former have a very much better prognosis than the latter, as has been well known since Callender's first report in

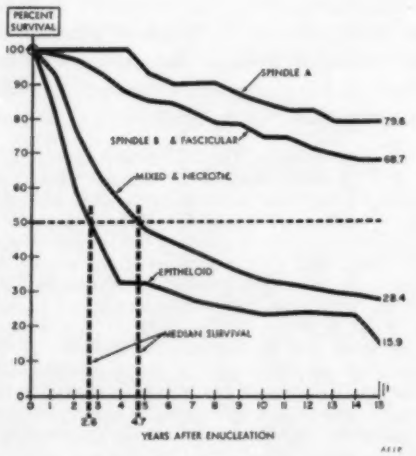


FIG. 36 (Zimmerman). Actuarial survival curves for 1,872 cases of malignant melanoma grouped according to cell type; curves based on data shown in Table 2. (Neg. No. 60-5499-2).

TABLE 2

MALIGNANT MELANOMA OF THE CHOROID AND CILIARY BODY ACTUARIAL SURVIVAL RATES BY CELL TYPE FOR LIVING VERSUS TUMOR DEAD

(Based on a study of 1,872 cases)

Interval from Enucleation to Last Known Status (yr.)	Spindle A	Spindle B and Fascicular	Mixed and Necrotic	Epithelioid
Under 1	100.0	100.0	100.0	100.0
1– 2	100.0	98.6	92.5	83.3
2– 3	100.0	96.3	76.6	59.1
3– 4	100.0	93.2	63.8	43.4
4– 5	100.0	88.6	55.5	32.3
5– 6	93.1	85.6	47.6	32.3
6– 7	90.2	83.4	44.5	30.3
7– 8	90.2	81.9	41.8	27.8
8– 9	90.2	79.4	38.7	27.8
9–10	86.6	78.5	36.3	27.8
10–11	84.6	75.1	33.7	23.9
11–12	82.4	73.6	32.9	23.9
12–13	82.4	71.9	31.5	23.9
13–14	79.6	70.6	30.2	23.9
14–15	79.6	68.7	29.9	23.9
15 and over	79.6	68.7	28.4	15.9

1931. These new data, however, reveal the spindle A tumors to be less benign than was once believed. These appear to be much more slow-growing tumors, requiring follow-up for longer periods to detect their lethal nature. During the first four years there were no deaths from spindle A tumors, while approximately 11 percent of spindle B, 44 percent of mixed and necrotic, and 68 percent of epithelioid melanomas proved fatal. After the first five years, however, the death rate of patients with spindle A melanomas paralleled that of patients with spindle B tumors. Likewise, the difference in prognosis of patients with the more malignant tumor types (epithelioid, mixed, and necrotic) was most clearly demonstrated during the first five years, after which the death rate paralleled that of patients with spindle cell tumors.

From these data we may make the following contrasting generalization: (1) more than half of the patients whose tumors are of the epithelioid, mixed cell, or necrotic types will die within five years, and more than three fourths will be dead within 15 years; while (2) less than one third of patients with spindle cell melanomas will have died even after 15 years.

Dr. Tom McKenzie, toward the end of his Academy-sponsored fellowship at the AFIP last year, initiated a new clinicopathologic study of the retinoblastoma cases contributed to the Registry prior to 1956. Most of the patients have been traced and the data are still being analyzed by our statisticians, but I can give you a few preliminary results that are of interest. From the curves shown in Figure 37 and the data presented in Table 3 we can make several interesting observations concerning the prognostic significance of optic nerve extension. Invasion of the optic nervehead up to but not beyond the lamina cribrosa (stage 1) appears to have no prognostic significance, for when compared with those tumors that have not invaded the nervehead, the respective survival curves can almost be superimposed. Extension beyond the lamina cribrosa, however, and involvement of the nerve at the plane of surgical transection (stages 2 and 3, respectively) do significantly worsen the prognosis. If we compare those cases in which there is no extension beyond the

TABLE 3

RETINOBLASTOMA:
ACTUARIAL SURVIVAL RATES BY STAGE OF OPTIC NERVE INVASION FOR LIVING VERSUS DEAD WITH TUMOR BASED ON A STUDY OF 300 CASES

Interval from Enucleation to Last Known Status (yr.)	No Invasion	Invasion			
		Stage 1	Stages 2+3	Stage 2	Stage 3
0– 1	100.0	100.0	100.0	100.0	100.0
1– 2	95.8	96.5	65.4	82.6	53.1
2– 3	91.6	93.0	57.2	73.9	45.3
3– 4	91.6	91.2	49.9	65.2	39.1
4– 5	91.6	89.4	47.2	63.0	36.0
5– 6	91.6	89.4	47.2	63.0	36.0
6– 7	91.6	89.4	47.2	63.0	36.0
7– 8	91.6	89.4	47.2	63.0	36.0
8– 9	91.6	89.4	47.2	63.0	36.0
9–10	91.6	89.4	47.2	63.0	36.0
10–11	91.6	89.4	47.2	63.0	36.0
11–12	91.6	89.4	47.2	63.0	36.0
12–13	91.6	89.4	44.2	55.6	36.0
13–14	91.6	85.2	44.2	55.6	36.0
14–15	91.6	85.2	44.2	55.6	36.0
15 and over	91.6	85.2	44.2	55.6	36.0

lamina cribrosa with those in which the tumors have infiltrated the nerve beyond the lamina, we find that there is only about a 10-percent mortality in the former while more than half the latter are dead within three years. The curves are of further interest because, in all groups considered, the curves become flat after the first three years. This suggested an analysis of the time interval between enucleation and death in the fatal cases (table 4). This revealed that more than half the deaths occurred in the first year and all but nine percent within the first three years. The very significant way in which choroidal invasion influences prognosis is shown in Table 5. Only six of 108 cases without choroidal invasion proved fatal, while almost half of 128 cases with choroidal invasion died.

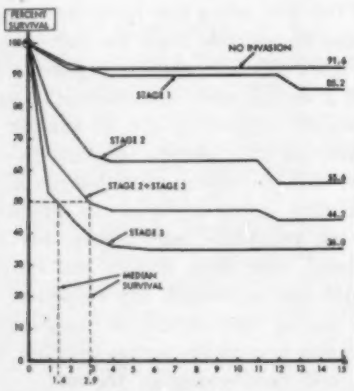


Fig. 37 (Zimmerman). Actuarial survival curves for 300 cases of retinoblastoma grouped according to stage of optic nerve invasion; curves based on data shown in Table 3. (Neg. No. 60-5499-1).

As most of you know, the Registry collection has not only provided much other valuable information concerning neoplasms but has also aided investigators who have been interested in many other problems. Two of the most significant contributions which have come out of the Registry collection were made possible by Mrs. Wilder's very exhaustive investigations in the field of intraocular inflammation, which led to her

TABLE 4

RETINOBLASTOMA:
DURATION FROM ENUCLEATION TO DEATH

Years	Number	Percent
Total deaths	78	100
Within 1 yr.	46	59
1 to 2 yrs.	15	19
2 to 3 yrs.	10	13
3 or more yrs.	7	9

TABLE 5

RETINOBLASTOMA:
EXTENSION INTO THE CHOROID

Degree of Involvement	Total Patients	Last Known Status			
		Dead		Alive	
		No.	%	No.	%
Moderate to marked	83	53	64	30	36
Slight	45	10	22	35	78
None	108	6	6	102	94

discovery that two parasitic diseases (toxoplasmosis and visceral larva migrans) account for more eyes that have been lost to the ophthalmic pathology laboratory than have tuberculosis and syphilis.

Time does not permit me to review the many pieces of research that have been made possible by the Registry but, to aid the interested reader, I have appended a bibliography arranged chronologically which includes most of the significant contributions that have been made by workers who have used the Registry collection.

THE FRIEDENWALD REPORT

In 1949 Dr. Jonas S. Friedenwald made a thorough analysis of the functions and problems of the Registry. These were considered under the three headings of (1) diagnostic service, (2) educational activities, and (3) research.

1. *The diagnostic service in ophthalmic pathology* had grown to an annual workload of about 1,700 whole eyes plus 700 biopsy specimens and/or sectioned eyes, and there were reasons to fear a further increase in the accession rate in the years ahead. Friedenwald believed such a routine workload to be about twice the optimum needed for training purposes. On the other hand, he recognized the very great value of the diagnostic service rendered to civilian ophthalmologists by the Registry, and for this reason, he did not favor any abrupt curtailment of this service. The heavy workload was burdensome to the technical and secretarial staff, and the already great backlog in the laboratory was increasing at a rate of about 200 eyes per year! The quality of the work was considered "superb" but there were simply not enough technicians to keep pace. Because of this shortage, it was impossible to develop a greater variety of special staining methods and to apply new histochemical techniques to ocular histology and pathology. Friedenwald therefore concluded:

> If a serious effort is to be made to catch up with the current backlog and to care for continuous growth, assuming that the present accession policy will not be immediately changed, there are, as I see it, only two possibilities. (1) The staff of the Registry could be increased by at least one more technician. This would be extremely difficult within the present limitations of available space. (2) A greatly increased proportion of the cases could be run through paraffin instead of celloidin. At the present time paraffin technique is used for rush diagnoses and for some fresh injuries and phthisis bulbis. It would appear that a much larger fraction of the accessions could be put through paraffin without seriously depleting the supply required in celloidin for teaching purposes.

Friedenwald also recommended an active decentralization policy—the development and support of other military and civilian laboratories for ophthalmic work. This he believed important, not only to free the staff at the Registry and give them more time for research work, but also as he stated:

> From the long run point of view of the advance of ophthalmic pathology, the maximal development of local diagnostic facilities is of major importance. Mail order diagnosis, no matter how good, can never be as enriching as the direct mutual consultation of the clinician and the pathologist. The more widely diagnostic responsibilities are disseminated, the more chance there is for the development of new concepts and new techniques. A maximal fruitfulness will, however, be achieved only if the local laboratories are closely affiliated with the Na-

tional Registry. It would appear that the Ophthalmic Pathology Club could be developed toward the goal of more active affiliative relationships.

Several of Friedenwald's recommendations have since been put into effect. An ophthalmic pathology laboratory was established at the Fitzsimons Army Hospital in Denver in 1953 by Lieut. James Duke. When Duke left the Army, Capt. Frederic R. Carriker continued the work. In 1954 another laboratory for ophthalmic pathology was activated at the 6th Army Area Medical Laboratory by Lieut. Alan Snyder. These laboratories not only received specimens from military installations in their respective geographic areas, but they also were sent many old "back-log" cases from the Registry. At that time a number of new civilian laboratories were established and older laboratories were expanding. Meanwhile additional technicians were assigned to the ophthalmic pathology laboratory of the AFIP, and in 1955 the laboratory and Registry moved into its new building on the grounds of the Walter Reed Army Medical Center, where larger and better facilities were available. Before leaving the old Museum building, the technical staff had begun to experiment with the paraffin technique for sectioning whole eyes. Since then they have mastered this procedure and the much more time-consuming celloidin method has been used only for selected cases.

The net result of all these developments between 1950 and 1955 was to reduce significantly the accession rate and virtually to eliminate the backlog. During the five-year period, 1955-1959, the average total annual accessions was down to 1,725 cases (almost to the level recommended by Friedenwald), and of these, the number of whole eyes averaged 976 (compared with 1,700 at the time of Friedenwald's report). The backlog of unfinished diagnostic work was gradually reduced to 391 cases at the end of 1959 from the record high of 3,459 cases at the end of 1953.

2. *The educational activities* of the Registry were also considered at length in Friedenwald's 1949 report. He stated:

> The fellowship posts represent the highest training facilities which the Institute can contribute, and a major effort should be made to bring this training up to the maximal possible level. Trainees should not be accepted for periods of study of less than one year and as soon as possible opportunities for apprenticeship in experimetal research and for clinical correlation should be developed to enrich the instruction.
>
> In discussing the problem with the current groups of trainees, I received the distinct impression that they needed more basic training in general pathology than they were receiving, and that the conferences of the various departments of the Institute could profitably be extended to include more elementary training than at present. Within the Ophthalmic division the pressure of the present diagnostic load is such that, in order to save time, each trainee works up the final report on his cases in private with Mrs. Wilder, and the rest of the group do not have the opportunity to participate in these discussions.
>
> Though facilities for research within the vast collection are readily available to the trainees, not much use has so far been made of these opportunities and a more active stimulation in this direction would be desirable. While the trainees enter the Institute with little or no training in ophthalmic and general pathology and are not qualified to undertake independent research, they could with great profit be assigned to work on small scale problems under direction, and thus learn how to approach a research problem in the field of ophthalmic pathology. The burden of such teaching would undoubtedly be heavy on the staff of the Institute but would not be devoid of rewarding aspects.
>
> In order to keep as many facilities as possible open to the trainees, short-term visits by individuals who merely want refresher courses or preparation for the Board examinations should be discouraged. This is not meant to apply to the utilization of qualified individuals of the facilities of the Registry for short-term studies.

Since then the fellowship program has been developed to a considerable degree, partly by the Academy and partly by other organizations, especially the National Institute of Neurological Diseases and Blindness, the Heed Ophthalmic Foundation, and the Council for Research in Glaucoma and Allied Diseases of the Alfred P. Sloan Foundation. The AFIP has followed Friedenwald's suggestion and has discouraged those who wish to come for short periods of study and has urged a minimum of nine months.

During each of the past three years there have been three or four fellows who have come for periods of nine or more months of training, and the number of applicants for the next two years has exceeded the available accommodations. Friedenwald recommended "more active participation of trainees in formal teaching and in research." Each of the trainees gives one or two lectures in the annual AFIP course in ophthalmic pathology, and as the fellows progress in the program they assist in instructing the newer men in the routine diagnostic work. Participation in research projects is encouraged, and the majority of fellows in ophthalmic pathology at the AFIP do complete at least one project deemed worthy of publication.

A fine example of what can be accomplished in a relatively short period was demonstrated to me by Dr. Milton Flocks, who, upon completing his residency in ophthalmology, came to the AFIP for six months as a Heed Fellow in July, 1954. During this brief period Flocks initiated and largely completed two major projects based on Registry cases (a clinicopathologic study of 138 cases of phacolytic glaucoma, in collaboration with Littwin and Zimmerman; and a study of the size and shape of malignant melanomas of the choroid and ciliary body in relation to prognosis and histologic characteristics, in collaboration with Gerende and Zimmerman). In addition, he began a histopathologic study of the trabecula using tangential sectioning, which subsequently led to several publications (Flocks, 1956, 1958 and 1959).

Friedenwald found the Registry's loan sets to be in need of "reconditioning," and he suggested that these elementary sets be supplemented by more advanced sets. The latter, he believed, should be smaller sets covering more restricted aspects of ophthalmic pathology (for example, uveitis, glaucoma, ocular tumors). During the past decade a considerable "stock pile" of special cases has been prepared for ultimate use in rejuvenating old sets and for use in smaller special sets. Much time and effort is to be spent in completing this work, and we plan to use the Academy's fellows to assist in this endeavor.

3. *With respect to research based on the wealth of material* in the Registry, Friedenwald stated:

> Considering the abundance or perhaps overabundance of the available material, the research production in the Registry has in the past been extremely scanty. This is not meant to disparage the quality of the work produced. The classification of melanomas and the study of the relation between histologic findings and mortality represents a large contribution carried out in a long range and thoughtful manner, but the total research output of the Registry clearly indicates that relatively little time is spent by the staff or the fellows on research. Moreover, little use of the facilities of the Registry has up to now been made by outside ophthalmologists for research purposes.
>
> The small amount of research initiated and carried through by the staff must be considered from two points of view. In the first place the burden of routine activities especially in relation to routine diagnostic service has been overwhelmingly heavy. In addition to carrying the diagnostic load, Mrs. Wilder has been called on to make a large number of trips for formal teaching purposes. Each time she is away on such trips, it costs her several weeks of hectic effort to catch up on the diagnostic backlog. The difficulties of formulating and carrying through more than a minimum of research studies under these pressures are enormous. In view of these difficulties the scientific output of the Registry, small as it is, is a remarkable tribute to her industry and effectiveness.

This report was made just a few years before Mrs. Wilder presented the results of her great contributions to an understanding of the etiology of granulomatous inflammations of the eye. Her work, based entirely on an extensive review of the accumulated cases on file in the Registry, involved the application of a large number of special staining procedures in her search for microorganisms. This led, eventually, to a recognition of the fact that toxoplasmosis, in the adult as well as in the infant, is more important than tuberculosis as a cause of uveitis and blindness, and to the fact that a most important cause of "pseudoglioma" of the retina in children is a form of visceral larva migrans.

These and other important contributions

made possible by the Registry material do not, however, negate Friedenwald's criticisms and his optimistic recommendation that the only answer is "the enlargement of the facilities, the increase of the Registry staff, and a curtailment of the growth of routine diagnostic service."

The future?

Time has not been sufficient for me to give you a complete picture of all the current activity in ophthalmic pathology and research stemming from the Registry. I have intentionally kept this part of my presentation to a minimum, since our annual reports published in the *Transactions* of the American Academy of Ophthalmology and Otolaryngology (see Hogan, 1954-1959) together with the bibliography that I have appended will provide the interested reader with additional information.

I would like to spend the remainder of my time in suggesting certain activities of the Registry which I believe should be curtailed, expanded, or otherwise changed to the benefit of all of us interested in advancing ophthalmology and ophthalmic pathology. Again these may be taken up in relation to consultative service, education, and research.

1. Consultative service

I fully share the opinion expressed by Friedenwald (cited previously) that the volume of diagnostic work provided by the Registry at the time of his 1949 report was excessive, particularly in relation to the available staff. During the past decade, however, the volume has been decreased and the staff has been augmented so that the task is less burdensome. Our present volume is about optimum to provide ample new material for the trainees. I would, therefore, not recommend any further reduction in our accession rate. On the other hand, I would not consider it wise to increase our present diagnostic service for "routine" specimens.

There is, however, one group of "routine" specimens of which we have insufficient material. The Registry of Ophthalmic Pathology is composed almost entirely of surgical cases, and very little autopsy material is available for teaching and research. There are many relatively common medical conditions which we lack. For example, we rarely receive eyes from diabetic or hypertensive patients unless an important ocular complication (usually secondary glaucoma) is superimposed on the initial process. This one-sided development of the Registry as a Registry of "surgical pathology of the eye" should be curtailed and an effort needs to be made to obtain more autopsy specimens.

I believe it would be very wise, if it were feasible, to increase the proportion of "unusual" or "difficult" cases to "routine" specimens contributed to the Registry. This could be accomplished if more "routine specimens" (for example, recent trauma, phthisis bulbi, and absolute glaucoma) were sent to the many laboratories about the country that have expressed a desire to obtain more cases (see Hogan, 1955), and if these laboratories would forward to the Registry those cases considered unusual or particularly valuable for teaching or research.

I realize, of course, that it is tedious, time-consuming and expensive for the local laboratories to support the Registry in this manner. Extra slides, copies of the histories, copies of the reports, and subsequent follow-up histories in selected cases are required, and someone in each laboratory must take the time to prepare the cases for shipment to the Registry. It is only the enthusiastic appreciation of the value of a central Registry and what it can contribute that will promote the support of individual laboratory directors.

It is possible, however, that the Academy can aid in this program and by so doing also provide better experience for its trainees. There are a number of fairly large ophthalmic pathology laboratories throughout our country that have been active for a sufficiently long time that they, too, have an accumulated wealth of material. If the Academy's

fellow were sent to at least one such laboratory each year, he could assist the director of that laboratory in selecting appropriate cases for the Registry and in the preparation of the material for shipment to Washington. In fact, if he were to travel by private auto, he could bring the material himself. We have an historic precedent for this technique of building up the Registry, because in 1937 Mrs. Wilder made an extensive tour, visiting most of the Nation's leading ophthalmic pathology laboratories for the express purpose of collecting melanomas of the uvea. This led to the rapid augmentation of the Registry collection and soon made possible more statistically significant follow-up studies.

To do something of this sort each year would require additional financial aid from the Academy, and it would also require the enthusiastic support of the various laboratory directors. If such a plan were approved, I would recommend first a visit to those institutions such as Washington University in St. Louis, Ohio State University in Columbus, and University of California in Los Angeles where autopsy material has become relatively more abundant than at most other laboratories.

2. Educational activities

I have written to many people who, in the past, have been concerned with the Registry in one way or another, requesting assistance in planning for the future. All have emphasized the need for continuing and expanding the educational activities of the Registry, which, as I indicated earlier, include the subtle individual type of teaching provided by our detailed descriptive reports to contributors, on-the-job training of physicians and technicians, preparation of loan sets and atlases, and group instruction at formal courses.

Our own training of fellows at the AFIP has not been entirely satisfactory because of the lack of a sufficient number of experienced staff pathologists to supervise all the activities. Friedenwald pointed this out at the time of his 1949 report, and it is just as true today—perhaps more so because of the increased demand for such on-the-job training.

Here, again, the Academy could help out. I would like to see the Academy sponsor a series of "resident consultants in ophthalmic pathology"—experienced teachers who would come to the AFIP for periods of two to four weeks to assist the chief of the Ophthalmic Pathology Branch in training the fellows. During such periods the resident consultant might give a few lectures or seminars, but his main service would be to help review the routine pathology reports being prepared daily by the trainees on the recently received specimens. During such periods of duty at the AFIP, he would also be encouraged to utilize the Registry material for his own research interests. Such consultants might also assist in preparing some of the advanced type of loan sets of slides on such special subjects as uveitis, vascular diseases, corneal dystrophies, and unusual tumors.

The practical problems we face in developing such a program are obvious: (1) the most experienced and qualified teachers are often too busy at home to get away for such long periods as two to four weeks, and (2) the program would require financial support. I feel optimistic, however, and believe that there are a sufficient number of good teachers and investigators in ophthalmic pathology who would be willing to give that much of their time every few years to promote such a program, particularly if they themselves could profit by the experience, as I am sure they would, by utilizing the material and facilities of the AFIP which we would make available to them. As for the Academy's supporting such a program, I am again confident because, if successful, its cost would be slight in comparison with its ultimate value. The better training of our young men, the cross-fertilization provided by having teachers and investigators come and go, and the increased utilization of Registry material for teaching purposes (study set, training manuals, and

so forth) and research would certainly justify continued support.

I have several times mentioned preparation of special study sets to cover more restricted fields. What I have in mind concerns more than histopathology. There is a definite need to correlate the clinical manifestations of certain diseases with their pathologic anatomy. With the ever-increasing use of photography by ophthalmologists, we are now in a much better position to present the clinical appearance as well as the histologic characteristics of many conditions. I envision our loan sets of the future as including Kodachrome slides illustrating the clinical appearance of many of the same lesions used for preparation of microslides and being accompanied by appropriate case histories, descriptive data, pertinent discussion, and references.

To accomplish this ambitious task will, of course, require better-than-ever support by all of you. Always send in to the laboratory good case histories and whatever illustrations are available at the same time that you contribute your specimens. This should be done not only when cases are sent in to the Registry at the AFIP but also when you send specimens to your local laboratory. Remember that most of your local ophthalmic pathology laboratories are operating in co-operation with the central Registry. They aid us greatly in winnowing the material for the most valuable cases for teaching and research.

Such a plan for better teaching sets will also require added man hours of service by qualified teachers to select cases and prepare the descriptive material. It will also be costly and will need the Academy's financial support.

Recently, in a discussion of the future of our Registry, Col. Joe M. Blumberg, scientific director of the American Registry of Pathology, suggested that we consider a great expansion of our educational program. There are vitally important new horizons for us to look toward in other lands. From an international viewpoint we are, today, in about the same stage of development as was ophthalmic pathology in the United States 40 years ago when Gradle and Callender began to develop their ideas for a national center.

There are two very important reasons why we should turn our attention toward other less privileged countries. From a selfish point of view, we need to know more about their medical problems and we need to obtain their pathologic material for our Registry (just as it was once considered so important by Gradle that every American ophthalmologist send in his specimens to Washington). One might presume that at the Armed Forces Institute of Pathology we would have an excellent collection of pathologic eyes representing virtually every known ocular disease to which man and animals are susceptible, obtained from all parts of the World. This is what we should have, but we do not. Actually, ours is a rather provincial Registry. Material from cases of trachoma, keratomalacia, phlyctenular keratoconjunctivitis, and many other ocular diseases that are still so extremely important in certain areas, is virtually unavailable for study and research.

In addition to these epidemic diseases, there are other special problems. I would like to tell you briefly about three examples in the field of neoplasia that, on the basis of random observations made in the pathology laboratory, deserve special study. It has been our experience that true infiltrative squamous-cell carcinoma is a rare conjunctival lesion in the United States. However, in the limited material we have received from contributors in Pakistan, we have been impressed by the apparently greater incidence of this epibulbar cancer. We have even seen a case of bilateral squamous carcinoma in a 10-year-old boy. Whether this is the result of genetic factors or environmental exposure to some carcinogenic agent is obscure; in fact, we do not even have enough information to know whether the observation of a seemingly high incidence of such tumors in Pakistan is valid. Similarly, in the limited material we have received from one large

city in South America, we have repeatedly been impressed by the disproportionate number of cases of retinoblastoma and the paucity of melanomas. Finally, I would like to tell you of a fascinating group of cases Dr. William Spencer has received at the University of California:

During 1959 Dr. M. D. Hursh of the Sudan Interior Mission Hospital in Kano, Nigeria, contributed to the Ophthalmic Pathology Laboratory of the University of California five cases in which there was such massive lymphoid infiltration of the orbital tissues that a diagnosis of malignant lymphoma seemed justified in each instance. In two cases, the lids and orbital tissues were involved, in two others the lids, orbital tissues, and uvea were affected, and in the fifth the lacrimal gland was greatly enlarged. Since lesions of this type are seen so rarely in the United States, Dr. Spencer was anxious to obtain more information about these patients. Dr. Hursh informed him that by strange coincidence two of the patients came from the same locality, "strictly bush with no doctors or hospitals," and that they had died within three months after enucleation. At the time of enucleation neither patient had shown evidence of generalized lymphomatosis and the cause of death remains obscure.

From the foregoing, it is evident that we should develop an interest in geographic pathology of the eye in order to provide ourselves with needed materials for teaching purposes and to broaden our knowledge of the etiology, epidemiology, and pathogenesis of various ocular diseases. But, possibly, this rather limited and selfish point of view is not the most cogent reason to expand the Registry program internationally.

We have reasons for believing that there exists in many parts of South and Central America, Asia, the Middle East, and Africa a fervent desire for better medical education and teaching aids of all types. The potential which we have for promoting international good will by means of medical education is expressed in a letter which Col. Blumberg recently received from the recipient of some study material in one of our neighboring Latin American countries:

> I am very grateful for the histopathology slides. Your collaboration not only helps in a cultural plan but demonstrates to the alumni of the Faculty that it is only propaganda what the Communists say that *North American Army is only another instrument of Yankee Imperialism.* By the above you might form a clear idea why this is significant to me and to those who practice Democracy.

Some of us believe that the American Registry of Pathology can do a great deal toward promoting genuine respect for the United States, as can each of the national societies which sponsor one or more of the constituent registries. Furthermore, as I implied before, there will be considerable "feedback" in the form of an increased number of cases contributed, better histories, more complete epidemiologic data, longer follow-up reports, and so forth.

I would give this proposed expansion of the Registry into the field of "geographic ophthalmic pathology" a high priority on the list of projects which the Academy should sponsor. A recent development in histologic technique has made possible the distribution of microscopic sections by first class mail at minimal expense and without fear of breakage (Ambrogi, 1960). It is now possible to mount and seal stained histologic sections in plastic sheets that can be folded, crumpled, or crushed without damage to the sections. Thus a whole teaching set of 100 sections can be assembled on about a dozen sheets of plastic (7.0 by 10 inches) which together with separating sheets of paper weigh about the same as five sections mounted in the usual fashion between glass slides (less than two ounces). Upon receipt at a medical center in some distant part of the world, the individual sections may then be cut out and mounted between glass slides in the usual fashion. Good histologic and cytologic detail may be obtained and the method can be used for mounting celloidin as well as paraffin sections.

3. Research

There is only one type of research that can be carried out by the Registry better than by any other organization with which I am familiar. This is the long-range follow-up study of remarkably large series of cases. I am very proud of our "detectives" who have tracked down patients even after their own ophthalmologists had considered them permanently "lost-to-follow-up." People like Miss Eleanor V. Paul, my assistant, Mrs. Evelyn C. Espeut in our follow-up unit, and Miss May Fraker and Mr. B. L. Parnell in our statistical analysis unit make this work possible. I really do not believe there is a comparable organization anywhere else. For this reason, it is extremely important that we continue to use our great storehouse of accumulated cases that have been followed so carefully over the years and to utilize our remarkable organization to obtain the maximum information for the benefit of our patients, just as Dr. E. A. Codman planned to do when he organized the Nation's first national registry.

At this time I should like to acknowledge our sincere appreciation to all contributors to the Registry who have been co-operating with us, first by providing good clinical histories and illustrations at the time they send in specimens, and later by responding to our requests for additional data—particularly long-term follow-up reports. Without such co-operation the Registry could never have developed into what it is today. Now, I would be remiss in my duties as Registrar if I were to leave you with the impression that all our contributors are so helpful; unfortunately, such is not the case! This is directed to the comparatively small group of unco-operative contributors: please do not waste our time and yours by not sending in specimens if you cannot provide a history or are unwilling to help out later when we need more data.

Second in importance for the Registry are the more esoteric aspects of ophthalmic research, such as electron microscopy and animal experimentation, because these can be pursued wherever the research facilities and personnel are available and are not dependent upon the unique collection and organization available only to us in the form of our Registry.

With respect to the follow-up activities of the Registry, there is one important way in which the program could be developed to provide us with answers to some very perplexing questions that have been raised at recent Academy meetings. In opening the discussion of a paper presented at the 1955 meeting by Flocks and his co-workers, in which the thesis was advanced that small melanomas of the choroid have a better prognosis than do large tumors, Maumenee asked if anyone had followed a large series of patients with nevi of the choroid to determine how often these lesions would become malignant. At the 1957 meeting, a panel headed by Dr. E. B. Dunphy discussed "the diagnosis and management of intraocular melanomas." In summing up some of the ideas that had been expressed during the symposium, Dr. Dunphy stated:

> Finally, we feel that there remains a lot to be learned about the behavior of malignant melanomas of the uveal tract. This is often unpredictable in contrast to that of malignant melanomas of the skin, where a rapid down-hill course is usual. We all know that some patients who refuse enucleation go on for years in perfect health with no sign of metastasis, while in others metastasis occurs in spite of early enucleation. Is it possible that early metastasis actually occurs in all cases but that in certain ones the tumor cells are restrained from growing in their new environment by some factor as yet unknown? In other words, do we actually save life by enucleation? May it not already be too late? No one knows for sure; until we have more knowledge on the subject, we must assume that we do and act accordingly.
>
> At this point I would like to make a plea that every ophthalmologist make a special point to follow up his cases in which enucleation is not done and see what happens to them. Perhaps the American Academy of Ophthalmology and Otolaryngology might establish a registry to which such cases could be referred for periodic evaluation and follow-up. It is our hope that this will be done, for only by such a study can we get an answer to this perplexing question of whether or not enucleation really prolongs life expectancy.

I believe the Academy should give serious

consideration to establishing a registry of "living pathology," as suggested by Dunphy and his co-panelists. Many large clinics already are following patients with uveal nevi or melanomas—patients who have refused enucleation or for whom enucleation has not been recommended. But the number of such cases in any one clinic is small, and without a large central Registry we shall never really be able to formulate any definite ideas about the natural behavior of these lesions: the frequency with which choroidal nevi become malignant, the rate of growth of small tumors, and the incidence of metastasis from small and large melanomas.

In the past all the Registries of the American Registry of Pathology have had as a basic requirement the acquisition of microscopic slides, blocks, and/or tissue from which a pathologic diagnosis can be established. Thus, the establishment of a new type of Registry in which the cases being registered would not be documented by histopathologic diagnosis would require a change in our basic policy. I feel confident, however, that if the Academy were convinced that such a Registry should be established and if the cases being registered were well documented by good clinical histories, fundus photographs, visual field charts, and the clinical opinions of a panel of experts who periodically would review and reevaluate each case, arrangements could be made formally to establish this type of Registry.

We have already established informally and on a very small scale such a Registry to aid in establishing the natural behavior of a particular group of melanotic tumors of the optic disc (Zimmerman, 1960). For several years, Dr. Lee Garron and I have been following a group of such cases in which the involved eye was enucleated. Our histopathologic studies and the follow-up reports have convinced us that these are relatively (if not absolutely) benign tumors, but only the clinical course of these lesions would really settle the issue. Fortunately our friends in several cities have sent us excellent drawings, Kodachrome slides, visual field charts, and follow-up reports of their cases in which enucleation was either refused by the patient or not recommended by the ophthalmologist. As a result, we are slowly accumulating excellent data which support our contention that these are, in fact, benign melanotic tumors. I would like to show you a few examples of these tumors (figs. 38 and 39), if for no other reason than to invite you to send me additional examples. These are not common tumors and it will take us a long time to accumulate a sizeable series. Therefore, we need every case we can get and we shall appreciate your contributions to this special series.

I must emphasize that this special collection is a personal effort, not really an official function of the Registry of Ophthalmic Pathology. If, however, the Academy were sufficiently convinced of the value of such a registry of untreated tumors (especially choroidal nevi and melanomas) that long-term support would be guaranteed, I believe such an undertaking would be feasible.

4. Committee on Ophthalmic Pathology

The Academy's Committee on Ophthalmic Pathology has been a source of great encouragement to me personally, as have many other members of the Academy who, though not now on the committee, have great interest and confidence in the Registry and who realize its unique character and almost unlimited potential. To all these people, and in particular to Dr. Benedict, your efficient executive secretary-treasurer, I want to give my personal thanks. I think it is a remarkable tribute to both the Academy and the AFIP that, now after 40 years, the "union which had been effected between the Academy and the Museum" (Gradle, 1921) is as strong, healthy, and mutually dependent as it was at the beginning.

I do believe, however, that there is still room for growth and development, as I have

just indicated. Furthermore, I believe that the Academy's Committee on Ophthalmic Pathology should be more active in discharging its dual responsibilities to the Academy and to the Registry. During recent years the principal work of this committee has been (1) the organization and supervision of a team to prepare a second edition of the Academy-sponsored book, the *Atlas on Ophthalmic Pathology*, (2) stimulation of local ophthalmic pathology laboratories to accept an increasing number of specimens in order to relieve the Registry of some of its volume of routine diagnostic work, and (3) development of the training program in ophthalmic pathology at the AFIP. These have been large, important tasks and the committee's chairman, Dr. Hogan, in particular, deserves the appreciation of all of us for the time and effort he has given to this work. On the other hand, I believe this committee could be even more active in promoting increased utilization of the opportunities available through the Registry. I think it would be very healthy and profitable for all concerned if at least once every year each member of the committee would visit the AFIP in the capacity of a consultant and critic—to find ways and means of assisting the Registry's activities in order to achieve maximum productivity and more efficient operation.

5. Summary

In summary, I have made the following observations and suggestions (with which the director of AFIP concurs) for the Registry's future development:

a. Routine diagnostic work should be kept close to the minimum required to ensure adequate training of fellows.

b. Consultative work and the acquisition of difficult or unusual cases should be increased.

c. Efforts should be made to obtain more autopsy material and to encourage contributors in other countries to build up a collection of "geographic ophthalmic pathology."

d. Support of on-the-job training of fellows should be continued but not expanded, since our present capacity is already taxed, mainly by the shortage of qualified instructors.

e. A program of "resident consultants in ophthalmic pathology" should be started in

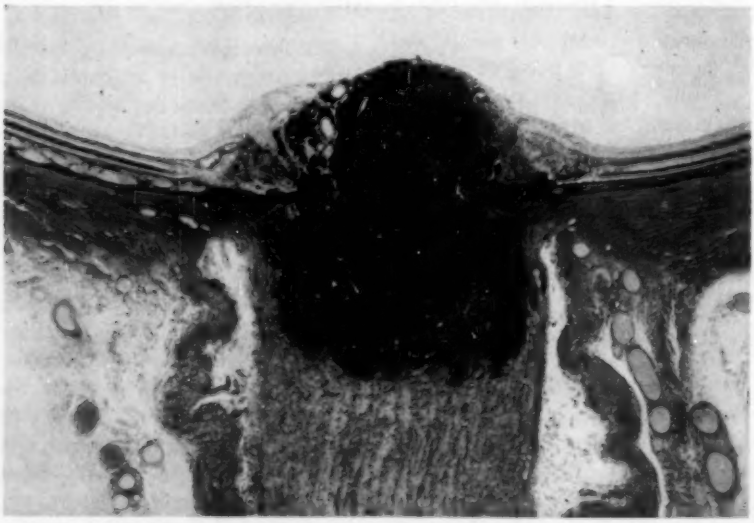


Fig. 38 (Zimmerman). Melanocytoma of the optic nervehead. (AFIP Acc. No. 507852, ×15.)

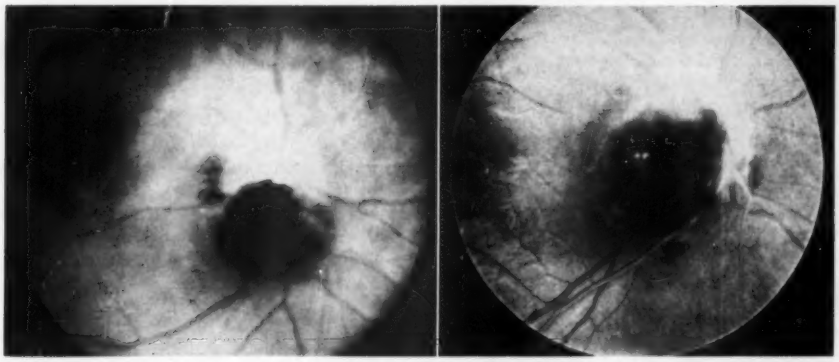


Fig. 39 (Zimmerman). Melanocytoma of optic disc. (Left) Clinical case being followed by Dr. Robert C. Schopp of Buffalo, New York, with no definite change during eight years of observation. (Neg. No. 57-5427.) (Right) Clinical case contributed by Dr. Manuel L. Stillerman of Chicago, Illinois, with no definite change during seven years of observation. (Neg. No. 57-5385.)

order to provide more instruction for the fellows and to promote greater utilization of the Registry material.

f. New study sets are required both to replace obsolete and damaged sets and to supplement the basic material with special collections to be accompanied by descriptive syllabuses, illustrations, references, and so forth. Distribution of such training aids to foreign countries needs to be encouraged.

g. Expansion of the Registry's follow-up program is important, since it affords a unique opportunity for this type of medical research. This activity needs continued and improved support from all contributors to the Registry.

h. The Academy's Committee on Ophthalmic Pathology should demonstrate greater interest and provide more consultation in guiding the future development of the Registry.

i. The Academy itself must augment its support of the Registry if we are to begin to realize the remarkable potential of this unique organization.

Armed Forces Institute of Pathology (25).

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Ophthalmic Miniature

After a glance at the methods hitherto employed for treating this condition (conical cornea), (v. Graefe) mentions that it occurred to him to excite ulceration and cicatrization in the centre of the diseased cornea. It is known that such a process will produce flattening of a cornea previously of normal curvature; and v. Graefe believed that the same action would be even more pronounced in an abnormal one. Patients with central leucoma in a normally curved cornea usually have much better vision, after a peripheral iridectomy, than is found in conical cornea of high degree, in which vision often sinks to 1/30, 1/40 or even less.

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NOTES, CASES, INSTRUMENTS

SUBRETINAL INTRAOCULAR HYDATID CYST

CLINICAL DIAGNOSIS AND SURGICAL TREATMENT

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Of the two types of intraocular cysts caused by the entozoan, cysticercus and echinococcus, the last type is exceptionally rare even in those countries where the echinococcus abound. It is still difficult to understand why this should be so, especially when compared with the extraocular implantation of this cyst. This fact has been emphasized by such well-known hydatologists as Devé,[1] Toulant,[2] and Lozano[3] and ophthalmologists as Greeff,[4] Duke-Elder,[5] and Demaría.[6]

The few cases mentioned in the literature of hydatidosis of the eye report histopathologic findings on an eye which has been enucleated with a diagnosis of secondary glaucoma or intraocular tumor. The cases cited by Gescheidt,[7] Griffith,[8] Werner,[9] Wood,[10] Scholtz,[11] Demaría[12] De Lieto Vollaro,[13] Litricin[14] and Rapaport, Mieres and Cicolini[15] come into this category. I should like to point out that the cases related by Gescheidt[7], Wood[10] and Scholtz[11] are not considered to be genuine cases of intraocular echinococcosis by the majority of authors who have studied this subject.

During a search through the literature, I did not find a single case of intraocular hydatidosis which had been clinically diagnosed, with the exception of that reported by Costi.[16] This patient was a 42-year-old woman with diminished vision in the right eye for 13 years, with detachment of the lower retina and a pyriform cystic tumor formation which, covered by the retina, crept over the vitreous body. Costi's diagnosis of subretinal hydatid cyst was based on the ophthalmoscopic characteristics and on a positive Weimberg's reaction and a positive but weak Casoni reaction.

CASE REPORT

The purpose of this paper is to report diagnosis of and operation on a case of intraocular hydatid cyst localized in the subretinal space in the macular region.

The patient was a 20-year-old woman who had lived all her life in the city of Buenos Aires. She first consulted me on December 1, 1958, because of loss of vision in her left eye.

External examination of the left eye was normal. Ocular motility was normal. Vision was hand movements. Ocular tension was 20 mm. Hg (Schiøtz). Gonioscopy showed a normal angle.

Ophthalmoscopic examination. The eyeball and peripheral and equatorial retina were normal. The macular region was occupied by an ovoid cystlike tumor which advanced toward the vitreous body with its longest axis vertical. Its surface was furrowed by retinal vessels coming from the upper and lower papillotemporal arterioles. Two minute hemorrhages of the retina were seen, located in the lower and upper poles of the neoformation (fig. 1). The tumor was whitish gray in color on two thirds of its surface, the remaining third being slate gray. A fringelike border separated these two zones. The two different colors covering the tumor were caused by the reflection and absorption of light radiations resulting from the differences in structure and density. The external border of this cystic formation was outlined by a pigmented area of retina

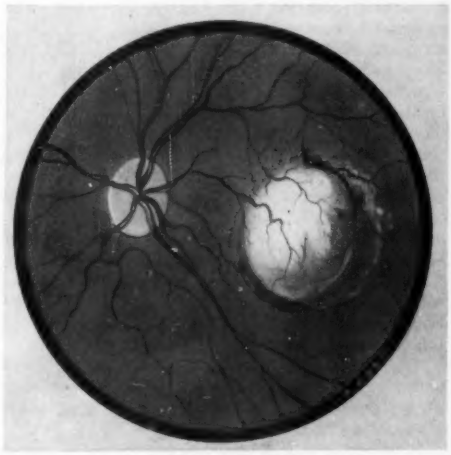

Fig. 1 (Sverdlick). Subretinal intraocular hydatid cyst.

in the shape of a new moon between the tumor and the periphery of the retina.

Biomicroscopic examination of the fundus added valuable details to the ophthalmologic examination. The tumor had a cystic covering protruding into the posterior camera. It was fixed, immobile and nontransparent. No internal structure could be seen or spontaneous or transmitted movements to the outer covering be observed. There were no undulations on its superficial surface. With the use of the diaphanoscope the light rays penetrated the cystic formation. No inflammatory changes could be seen in the vitreous body or in the intraocular structures.

All this led to a presumptive diagnosis of probable intraocular parasitic cyst. Casoni's[17-18] intradermic reaction proved positive (+) and Imaz Apathie and Lorentz'[20] reaction was also positive (++) and confirmed the probable diagnosis. The blood count showed 5.0-percent eosinophils. The result of the clinical examination was normal as was an X-ray examination of the chest.

The rapid growth of the tumor—approximately six months—and the results of the ophthalmologic and biomicroscopic examination, together with the positive Casoni and Imaz Apathie-Lorentz reactions, confirmed the diagnosis of subretinal intraocular hydatid cyst of the macula.

The diagnosis of subretinal cysticercosis was discarded because of the ophthalmologic, biomicroscopic and evolutive signs. Once the diagnosis of intraocular echinococcal entozoa was made, as conservative an operation as possible was planned. The progress made in the technique for treating small intraocular blastomas, using diathermic electrocoagulation as performed by Weve,[20-21] Safar[22] and Stallard,[23] to produce a covering layer of cicatricial chorioretinitis, suggested the following procedure:

Under general anesthesia external peritomy was performed from the 6- to 12-o'clock position. The external and inferior rectus muscles were disinserted to allow an ample operative field. The cyst was localized with the ophthalmoscope, the sclera was pushed aside with a blunt electrode, and superficial electrocoagulation applied. Sclerotomy was then performed, layer by layer, until the herniated choroid appeared. A No. 25.5 blunt needle attached to a syringe was inserted and 1.5 cc. of transparent, crystal clear fluid was aspirated. Still using the ophthalmoscope an intense barrage of electrocoagulation was applied to the tumor, after which the sectioned muscles were sutured and the wound in the conjunctiva closed. The postoperative course was without complication. Microscopic examination of the liquid obtained by aspiration showed no echinococcal hooks. The cyst proved to be sterile.

Ophthalmologic examination during the postoperative period permitted following the evolution of a pigmented cicatricial layer in the spot where the cyst had been located.

Comments

As mentioned by Demaría, Argentine physicians and surgeons have found hydatid cysts in every organ but the eye. The only two cases of intraocular hydatidosis reported in this country were found during histopathologic examination by Demaría[12] and Rapaport, et al.,[15] of enucleated eyes.

There is definite experimental proof of intraocular echinococcal entozoosis. Demaría[6] studied its ophthalmologic, parasitologic and physiopathologic evolution. He injected into the anterior and posterior eye of a rabbit material obtained from a hydatid cyst in a sheep. This produced hydatid cysts four months later in nearly all parts of the eye structures. These cysts were characterized by the lack of pericystic membranes, similar to cerebral hydatid cysts.

Devé,[1] under conditions similar to those in human infection where the echinococcal embryo arrives in the eye through the blood stream, inoculated a hydatid scolex and not an embryo. He injected 0.25 cc. of liquid taken from a hydatid cyst of a sheep into the extreme center of the left carotid artery, after having first ligated the carotid artery on the opposite side. A subretinal hydatid cyst subsequently developed. According to Devé, the intraocular hydatid cyst is the result of the cystic evolution of the scolex and is similar to the vesicular evolution of the echinococcus larvae, with all its histologic and biologic characteristics.

To return to the case here reported. How did the intraocular embolism of the embryo occur? We presume the mechanism to be: Once the egg of the taenia echinococcus reaches the stomach the digestive juices disintegrate its covering, leaving the embryo free. The diameter of this is between 22 and 28 microns. It then joins the blood circulation and follows the route of the ophthalmic artery, reaching the short posterior ciliary arterioles, the final dichotomic divisions of which form the choriocapillary network of the choroid, then it definitely establishes itself in the subretinal space, where the embryo becomes transformed into a cyst.

The special preference shown by the lar-

vae of the taenia for the subretinal space has, it would seem, a histophysiologic basis. The vascular connective organization of the choroid of human beings was studied with Rio Hortega's silver impregnation technique,[24] and the choriocapillary network was found to be formed by large endothelial tubes—those of the largest diameter being at the level of the macula. Precollagenous fibrils radiate from the walls of the capillaries, and, on becoming fixed to the walls of the neighboring vascular tubes, replace the myofibrils and play an active part in keeping the capillary lumen sufficiently open. It may be that these anatomic conditions facilitate the carrying of the echinococcal embryo to the subretinal space, as the macula is avascular and nourishes itself at the expense of the choriocapillary lamina.

Summary

A case of subretinal intraocular hydatid cyst located on the macula is reported. It is believed to be the first case diagnosed clinically and operated with this diagnosis to appear in ophthalmologic literature. The ophthalmologic and biomicroscopic signs in the fundus oculi, together with the results of the Casoni and Imaz Appathie-Lorentz' reactions, as well as rapid evolution of the tumor (six months) led to the definite diagnosis of echinococcal entozoosis.

The diagnosis of subretinal cysticercosis was discarded because of: (a) the immobility of the cystic growth; (b) its lack of transparency; (c) the absence of interior structures, as well as lack of spontaneous or transmitted movements to the outer covering; (d) the fact that there were no inflammatory changes in the retina and vitreous body; (e) its rapid evolution.

The liquid obtained by aspiration during the operation did not show any echinococcal hooks. It proved to be a sterile cyst.

Bmé. Mitre 1427.

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A PRESSURE-SENSITIVE CRYSTAL OSCILLATOR*

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CHARLES HORN, B.S.,
AND
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In recent years there has been a marked increase in the search for electronic applications to medicine; this has also been true in the field of tonometry; for example, Mackay and Marg's feedback-stabilized ferrite core tonometer[1] and the Nesterov, et al. pickup-plunger high frequency tonometer.[2]

We have joined the search for a pressure transducer through the special interest of one of us (D.E.N.) in the physical properties of crystals and have utilized some principles of crystalology in the construction of an efficient pressure-sensitive instrument.

It is well known that crystals can be used to translate mechanical motion into an electrical signal via their piezo-electric effect. This effect has been utilized in such common instruments as the crystal phonograph pickup and crystal microphone. On the other hand an *oscillating* crystal also has certain properties which might be used for a pressure transducer, as suggested by Mackay and Marg.[1] We chose to design, develop and build a tonometer based on the crystal as the transducer and are currently testing the prototype instrument.

If a crystal is made to oscillate electrically at a certain frequency, pressure on that crystal will cause a shift in the frequency of oscillation, and this shift will be a function of the pressure on the crystal. If this shift were linear with pressure, a useful instrument could be constructed.

Figure 1 shows the change in frequency of oscillation of the typical crystal plotted against applied pressure. The entire curve is not completely linear; if, however, the crystal is "pressure biased" into the region of the curve which has a constant slope, the response is linear.

The frequency-pressure curve is a characteristic of any particular thickness-shear mode crystal. The steeper the slope, the greater the effect of pressure on the frequency shift, and the more suitable the crystal for our purposes, all other factors remaining constant. Many crystals demonstrate this property, some better than others. At present we are using quartz (silicon dioxide). Concurrently a search is being con-

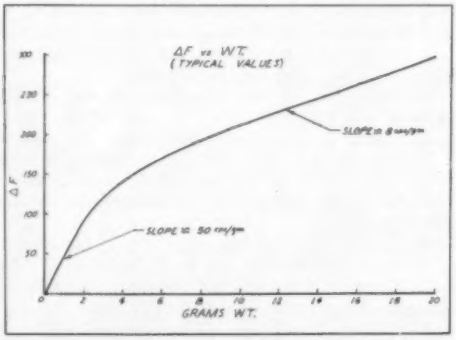

Fig. 1 (Newell, Rubin, Horn and Armaly). Curve demonstrating the frequency shift vs. applied pressure in a typical thickness-shear mode oscillating crystal.

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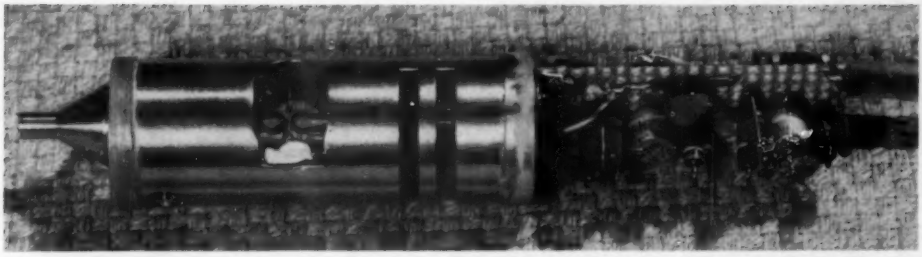

Fig. 2 (Newell, Rubin, Horn and Armaly). Photograph of the tonometer probe with its shield-insulator removed, revealing the glass rods pressing on the crystal and the transistorized Colpitts osciliator.

ducted by a group at the Department of Electrical Engineering at the State University of Iowa for an optimum material. The effect of varying the angle of section of the quartz crystal as well as the examination of other materials which exhibit more useful $\frac{\text{cycle shift}}{\text{mm. Hg force}}$ characteristics are being explored.

An undesirable effect on the crystal oscillation is the environmental temperature fluctuation. Quartz is less susceptible to this effect than are other materials. This obstacle has been controlled by allowing the crystal temperature to stabilize completely before use. By experimenting with temperature shielding and utilizing other crystals, we are confident this temperature effect can be completely suppressed.

The pressure exerted on the crystal must be at a point. If too large an area is pressed, the frequency shift is damped out. This fact precludes the use of the crystal itself as the direct contact against a globe in determining intraocular pressure as suggested by Mackay and Marg,[1] and necessitates the use of a "plunger" in a probe to transfer the pressure from a globe to the crystal.

The change in crystal thickness to produce a frequency change is infinitesimal. Exact measurement of this displacement would be extremely difficult but a calculated approximation yields the remarkably small movement of the order of one Angstrom (10^{-8} cm.)! This displacement is molecular in nature and not mechanical.

Figure 2 is a photograph of our probe with the shield-insulator removed. When the instrument is used as a tonometer, the probe tip is used to flatten the cornea until it is applanated over an area of three-mm. diameter. The actual "plunger" is 1.5 mm. Supposedly, when the "plunger" is fully applanated, the pressure acting on it is only the intraocular pressure. In a practical sense, however, corneal factors (for example, "compressibility") also must be considered. We plan to determine the significance of these factors and report them in a later publication.

Figure 3 is a drawing of the mechanics of the probe. The plunger is constructed of stainless steel. In this experimental model, the steel presses on a glass rod which in turn presses on the crystal. This extra link allows us to have a removable tip and thus perfect the tip-plunger design. Behind the crystal is another glass rod in direct alignment with the plunger. Any misalignment would lead to a shearing force on the crystal and distortion of the output. This alignment is easily accomplished and has been no problem.

As pictured in Figure 2, behind the mechanical transducer is a conventional transistorized oscillator (Colpitts design) with an emitter follower isolation stage. This is necessary to isolate the oscillator from cable variables and to provide an impedance match to the coaxial cable (73 ohm characteristic impedance). The cable terminates on the unit chassis and feeds directly into the multiplier section.

From the coaxial cable, a signal (the oscillating frequency) could be read directly (as

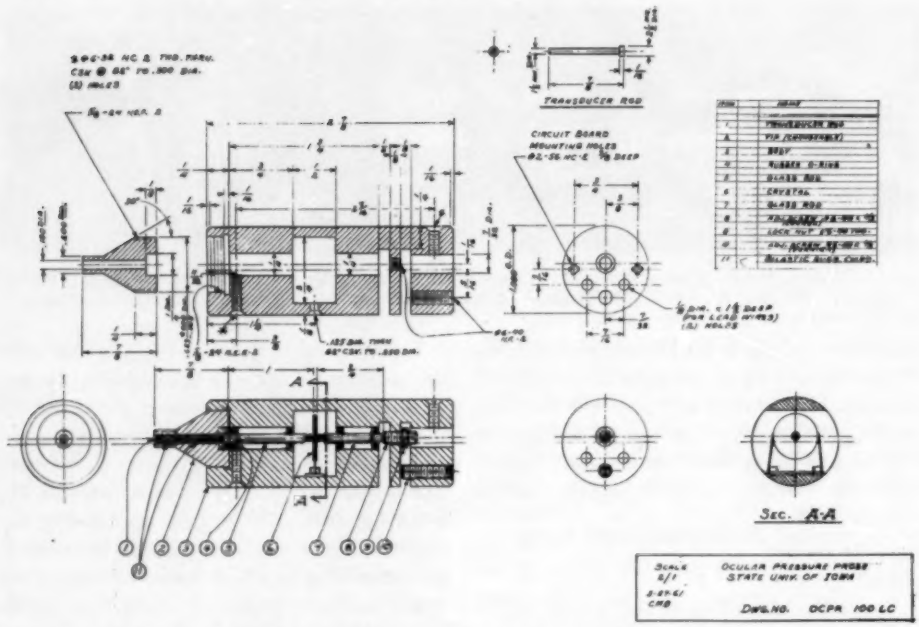

Fig. 3 (Newell, Rubin, Horn and Armaly). A drawing of the mechanical portion of the tonometer probe.

by a digital counter) and the shift from the rest-oscillation could be calculated, the shift being proportional to the applied pressure. Since the exact instant of registration of the "true" intraocular pressure cannot be known, it is necessary to feed the cable signal electronically into a standard recorder to obtain a smooth curve. The remaining electronics serve to convert the oscillator frequency into a voltage which is proportional to the change in pressure applied to the crystal.

Figure 4 is a block diagram of this instrument and the electronic components, which form a usable voltage, which can in turn be

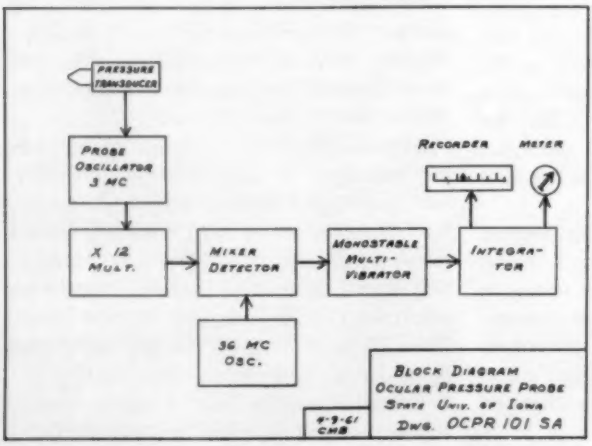

Fig. 4 (Newell, Rubin, Horn and Armaly). A block diagram of the electronic components of our pressure-sensitive instrument.

conveniently displayed on a recorder. A description will follow the layout of the block diagram.

The signal first goes to the multiplier stage which takes the incoming three megacycle oscillation signal (plus the change due to applied pressure) and raises it by a multiple of 12 in four stages to 36 megacycles plus 12 times the frequency shift due to the pressure. This multiplier factor can be easily changed to yield a wide range of pressure sensitivities.

Next the signal goes to a mixer which separates the frequency change due to pressure from the 36 mc. signal carrier on which it is imposed. This frequency difference is changed to a usable voltage by running it through a circuit which changes it to a series of constant energy pulses which vary in number as the frequency varies. These pulses are then integrated (summed) giving a voltage which is directly proportional to the rate at which the pulses occur. In other words, a change in frequency due to pressure is now available as a change in d.c. voltage, which can be fed into a recorder.

The instrument could be diagramed as three individual units by constants which represent the contribution of each to the sensitivity of the entire instrument. The first functional unit is the crystal oscillator and its constant would be in terms of cycles shift/mm. Hg force applied. The second unit is the multiplier whose constant can be any desirable number. The third unit is the voltage producing unit with a constant in terms of volts/cycle. We will call the constants K_o, K_m and K_v respectively. and define our sensitivity as volts/mm. Hg. Thus:

$$\text{Sensitivity} = K_o \text{ (cycles/mm. Hg)} \times K_m \times K_v \text{ (volts/cycle)}$$

At present our sensitivity is two millivolts per mm. Hg. As can be seen from the equation we can easily increase this sensitivity by increasing any one of the three unit constants.

The resolution depends on the response to small pressure changes of the crystal itself, and on the resolution of our recording instrument.

Figure 5 shows the curve obtained by our recorder when the probe is pressed against the cornea of an enucleated cat eye, and demonstrates the resolution of pressure effects at the probe. It is clear that this curve is similar to that obtained by Mackay, Oeschsli, and Marg.[5]

Figure 6 is a photograph of the electronic unit, probe with its shield in place, and two replaceable probe tips.

Our future plans include transistorizing the electronics, refining the mechanical design of the probe itself, investigating the effects of the tonometric procedure on the eye to be tested, evaluating the pressure curves obtained and calibrating them, and checking

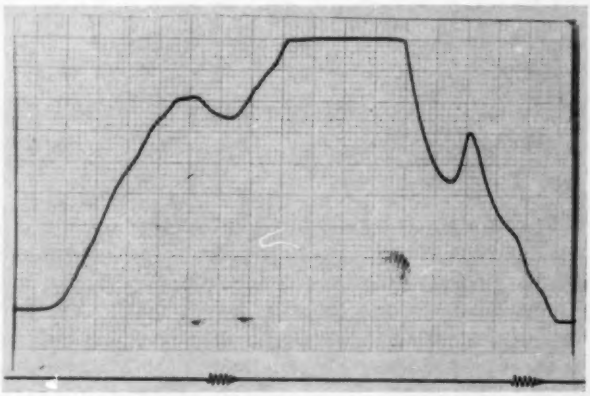

Fig. 5 (Newell, Rubin, Horn and Armaly). A typical recorded curve reflecting pressure, as obtained utilizing our probe as a tonometer pressed against the cornea of an enucleated cat eye. The time span of the entire curve is approximately 1.5 seconds.

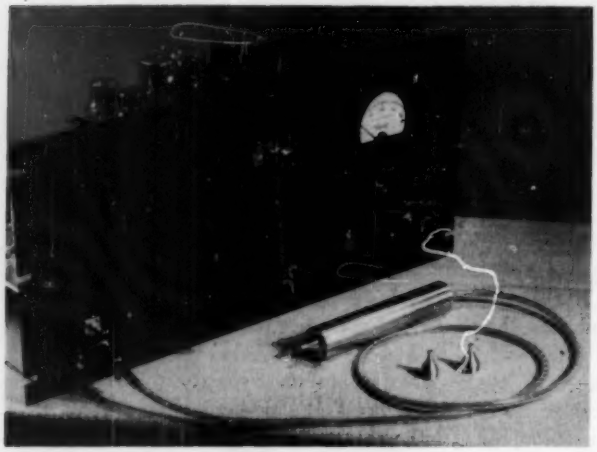

Fig. 6 (Newell, Rubin, Horn and Armaly). Photograph of the tube version of the electronic unit, probe with its shield in place, and two of the replaceable probe tips.

into other possible applications of the extreme sensitivity of this instrument.

Summary

A new pressure transducer is described. This instrument is fundamentally a pressure-sensitive crystal oscillator, the shift of frequency of the oscillation being proportional to applied pressure. The transducer is mounted in a probe suitable for tonometry and is extremely sensitive to small pressure changes with an infinitesimal mechanical displacement. The mechanics and electronics of the unit are described and future plans for investigation are outlined.

University Hospitals.

Acknowledgment

We wish to thank Dr. A. E. Braley and Mr. T. Hunter of the State University of Iowa for their support of the numerous projects which led to the construction of this instrument.

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A NEW PROJECTOR CHART

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Projector charts have changed little in the last 15 years. Aside from the addition of a few new slides, the basic concept is unaltered. The unit is bulky and generally gets in the way of the examiner. Turning and looking at the projector when changing the test pattern and again turning to look at the chart to make certain the proper figures are projected are major disadvantages. A mirror placed behind the patient or to the side may eliminate this second maneuver. Limitation of variety and choice of test figures is another disadvantage.

The purpose of the instrument here described is to provide a greater ease in projecting the chart and therefore less lost motion, as

well as increased flexibility of test pattern and objects as desired by the examiner. The cost of the equipment is also lower.

The basic unit consists of an automatic remote control 35-mm. slide projector and test slides. The Sawyer 500R and Airequipt Superba 66 are both adaptable to the purpose. The projector is placed at a convenient distance from the screen, depending upon the setup of the room. Slides are then made according to the distance of the projector to the screen, the focal length of the lens in the projector and the distance of the patient's eye to the screen. If the projector is placed near the screen, six to 10 feet, a four-inch focal length lens can be used. However, if it is placed farther than this a lens of longer focal length, five or seven inches, is more desirable.

Utilizing this information, slides of test figures of properly proportioned size can be made, using any combination of letters, numbers or other test figures. Single lines of 20/20 to 20/400 may be made and letters so spaced that the frequently bothersome crowding together of small letters may be overcome by equal spacing of the 20/20 figures, similar to the spacing of the 20/50 figures.

The magazine of the slide projector holds 36 slides. The test slides are placed in sequence in the magazine so that, by activating the changer, progressively smaller or larger slides will be shown. This eliminates the need to turn to check the projected figures with each change. A great variety of test lines may be made for 20/20 and 20/30 so that the patient cannot memorize the charts.

Duochrome slides for red-green testing and color-blindness slides may be incorporated into the battery of test charts. A limitless number of test slides can be devised, depending upon the examiner's desires.

The standard remote control unit supplied by the manufacturer of the projector, may be used for changing the slides and focusing by remote control. The power supply and off-and-on switch should be located convenient to the examiner. However, I found it expedient to construct a more permanent and durable switchbox as follows:

Power was run to the projector from a low-voltage unit placed near the projector and activated by an off and an on momentary switch. These two switches plus four more momentary contact switches were incorporated in a standard Bakelite switchbox and wired appropriately to replace the manufacturer's remote control unit. The switchbox was then located in a convenient spot near the examining chair for fingertip control.

Distortion, resulting from placement of the projector at an angle to the line of vision of the patient, may be overcome by turning the screen so that it is almost perpendicular to the line of projection and at an angle to the line of vision of the patient. This produces a square test pattern and no distortion.

188 Clinton Avenue (5).

Ophthalmic Miniature

The Bum's Mixture (Mistura Errabundi) has long been a favorite remedy at Bellevue Hospital for cases of recurrent indolence, and the undue attachment of healthy bodies to hospital wards. The New York Hospital claims to have something superior in the same line, which is called "The Undertaker's Revenge," and is an appetizing combination of copaiva, castor, ether, quinine, etc.

Med. Record, **25**:99, 1889.

SOCIETY PROCEEDINGS

EDITED BY DONALD J. LYLE, M.D.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

December 21, 1960

BITEMPORAL HEMIANOPIA

DAVID D. DONALDSON, M.D., presented a 56-year-old man who had suffered multiple skull and facial fractures on the left side when his head was crushed between the pilot house of a boat and the steel girder of a bridge. His left eye had been pushed 14 mm. into the orbit, due to multiple orbital fractures and loss of fat. Skull X-ray films demonstrated air in the ventricular system which nicely outlined the chiasm. Neurosurgical exploration revealed no brain damage and only a tear in the dura in the left frontal area, which was repaired. Eye examination some time after the injury revealed a vision of 20/20 in the right eye and 20/50 in the left eye. There was residual enophthalmos of the left eye, plus restricted ocular motility on the left and diplopia. He demonstrated a bitemporal hemianopia. Bitemporal hemianopia due to trauma has rarely been described.

WERNICKE'S SYNDROME

MAURICE VICTOR, M.D., presented a 39-year-old woman who had been an alcoholic for 11 years. She was admitted with Wernicke's syndrome and treated with a vitamin-free diet plus thiamine. On this regimen there has been marked improvement in ocular motility. During discussion of this case it was pointed out that only five percent of patients with Wernicke's syndrome have toxic amblyopia.

NONSYPHILITIC INTERSTITIAL KERATITIS

DAVID G. COGAN, M.D., presented a 14-year-old boy who several weeks before first being examined had developed trouble walking and vomiting. Thereafter he rapidly developed deafness in both ears which was marked in degree and had not improved since onset. As the deafness progressed difficulty in walking decreased. Two weeks after the onset of deafness his eyes became red and photophobic. The only abnormality on routine laboratory testing was a highly elevated white count which is characteristic of this syndrome. Eye examination showed patch infiltration of the corneal stroma which has been variable day to day. This type of infiltration differs from the luetic type of interstitial keratitis in that it is variable from day to day, there is no intraocular involvement, and there is no swelling of the stroma. There is also much less vascularization in this type of keratitis than in luetic interstitial keratitis. This patient is typical of a syndrome first described by Cogan in 1945 which he has called nonsyphilitic interstitial keratitis with vestibuloauditory symptoms. The visual aspects carry a good prognosis but the auditory aspects do not. There is no adequate treatment for this condition, nor has an etiologic agent been discovered. Serologic tests for syphilis are always negative.

CATARACT SURGERY

EDWIN B. DUNPHY, M.D., discussed some of the complications of cataract surgery and their management. Retrobulbar hemorrhage following injection of anesthesia calls for cancellation of surgery. Hemorrhage which occurs subconjunctivally as a fixation suture is being placed around the superior rectus can often be controlled by tightening the fixation suture around the muscle.

If a cataract knife is introduced upside down, it is best to withdraw the knife and reinsert it. If the chamber is not formed, a small incison can be made, using scissors to complete the section. Sutures placed too deeply should be withdrawn and replaced.

Continued prolapsing of the iris following corneal section forebodes trouble and measures must be taken to reduce any pressure on the globe.

An eye in which expulsive choroidal hemorrhage occurs can sometimes be saved by rapid drainage of the subchoroidal space. One may be forewarned of this complication by a complaint of sudden severe pain on the part of the patient who up till this point has been satisfactorily anesthetized.

Posterior dislocation of the lens at the time of application of forceps or cystotome requires extraction by lens loop. If the lens falls into the vitreous, it may be irrigated therefrom by a strong stream of saline directed back into the eye. If this procedure is unsuccessful, the lens may be left in the vitreous cavity and, if the capsule has not ruptured, the eye will tolerate the lens indefinitely; however, if the capsule has been ruptured, the eye is usually lost.

Loss of completely fluid vitreous is of no consequence. Loss of formed vitreous is a serious complication. When formed vitreous is lost, it is necessary to release all tension on the globe to allow the vitreous to retract into the globe. If formed vitreous is lost before the lens is extracted and a firm hold is had on the lens capsule, then the lens may gradually be withdrawn from the eye by traction alone. If the lens is not firmly held, it should be removed with a loop. Following the loss of formed vitreous a full iridectomy should be done, if this has not already been done.

Rupture of the lens capsule cannot be considered a real complication but rather a disappointment. If anesthesia and akinesia are still good, it is important to remove as much of fragmented capsule and cortex as possible. The use of small forceps to pick up pieces of capsule on the iris surface is justifiable but, when used in the pupil, this procedure carries certain dangers.

Nausea occurring during cataract surgery can sometimes by counteracted by inhalation of oxygen. If vomiting occurs, the patient's face should be turned away from the operated eye. If vomitus should enter the eye before the lens has been removed, the eye should be irrigated and the wound closed and further surgery postponed. If vomitus enters the eye after removal of the lens, the eye should be irrigated and large doses of antibiotics should be used prophylactically.

Glaucoma surgery

Paul A. Chandler, M.D.: Nearly all patients with angle-closure glaucoma are operated on no matter what the stage of the disease. In early stages all closure can be prevented by peripheral iridectomy; in later stages further closure of the angle can be prevented. In some patients who generally have dilated pupils following an acute attack of glaucoma, or a dilation in one meridian, the pupillary block is permanently relieved. In these cases iridectomy will add nothing further.

In angle-closure glaucoma, if all or a large portion of the angle is open gonioscopically, iridectomy is the treatment of choice. If one third or more of the angle appears to be closed by synechias, a filtering operation is necessary. In cases in which it is not possible to determine by gonioscopic examination whether or not sufficient angle is open for iridectomy to be effective, it still can be tried if the tension can be normalized by miotics alone; if the C value was high before glaucoma appeared (as determined by tonography); or if gonioscopy at the time of surgery after the chamber is deepened shows the angle to be more than two thirds open.

Dr. Chandler then described his technique of peripheral iridectomy. He cautioned against the use of scleral cautery in doing peripheral iridectomy so that the danger of producing a filtering scar would be minimized. He also cautioned against making too small an iridectomy in order to avoid obtaining only the stroma of the iris and leaving the pigment epithelium intact and therefore, in effect, creating no iridectomy. Following peripheral iridectomy it is important to ob-

serve carefully for signs of iritis and, if they are present, to treat actively with mydriasis and the usual steroids. If a flat chamber occurs, it must be reformed immediately in order to prevent permanent peripheral anterior synechias.

Everyone has his own indications for surgery in open-angle glaucoma. It is axiomatic, however, that, in the presence of advanced cupping and atrophy, surgery must be done to keep the tension in the teens or low twenties (1948 scale), since eyes with advanced glaucoma will not tolerate tensions higher than this. The operation of choice in open-angle glaucoma is the one with which the individual surgeon is most familiar. In the presence of shallow chambers, trephination may lead to incarceration of the lens in the trephine opening. Dr. Chandler personally favors trephination in young patients and in cases of so-called low-tension glaucoma where marked hypotony is desirable.

Certain points of surgical technique which Dr. Chandler has found helpful were described. The first is to make a slanting incision in the lower portion of the cornea with a needle knife as the first step in any surgical procedure for open-angle glaucoma. This incision is useful in many ways. In trephining operations it is helpful to deepen the chamber markedly, with saline introduced through this opening prior to trephining the sclera. (In trephining the sclera, it is extremely useful to have a Grieshaber trephine with a guard.)

Deepening the anterior chamber through the slanting corneal incision is also useful in cases in which one prefers to use a knife or keratome for making an incision in iris inclusion operations or sclerectomies.

At the conclusion of any filtering operation it is useful to inject saline through the slanting corneal incision in order to determine whether or not the bleb can be formed. If the bleb cannot be formed by this procedure, there is no chance of a successful operation. It is then necessary to examine the wound and correct any obstruction to the opening which may exist.

If buttonholing of the conjunctiva occurs during preparation of the flap, the effect of this can be avoided by moving to a different site to make the scleral incision. If the conjunctiva is buttonholed after the sclerectomy has been made, or if the buttonhole is first noted after sclerectomy has been done, it is possible to convert this round hole into a narrow slit by pulling the conjunctiva around the limbus and tacking it to the episclera in an area remote from the wound. This technique has been extended to cases in which no buttonhole has been formed in order to tighten the conjunctiva over the sclerectomy and appears to have reduced the incidence of postoperative flat chambers.

In angle-closure glaucoma requiring a filtering operation it is essential to open the sclera by an ab-externo incision.

Suturing of the conjunctival wound is important in avoiding flat chambers. Dr. Chandler feels that the development of flat chambers postoperatively is the largest cause of failure of filtering operations. A pressure dressing is useful in helping to form flat chambers. If a chamber remains flat longer than five days, there is not only danger of peripheral anterior synechias occluding the angle but also of failure of the bleb. If the chamber is formed surgically by release of subchoroidal fluid and injection of saline into the anterior chamber and the bleb does not form as the anterior chamber is expanded, forceful injection of saline will sometimes suddenly open the bleb and lead to successful operation.

Urea in acute angle-closure glaucoma

Kevin Hill, M.D., Jeremy Whitney, M.D., and Robert Trotter, M.D.: The effects of intravenous hypertonic urea on the tension in 13 patients with acute elevation of intraocular pressure were evaluated. The intraocular pressure was reduced in each of 13 eyes with acute angle-closure glaucoma. In 10 eyes, the tension was lowered to 23 mm. Hg or less. In three other eyes the tension fell only to 40 to 45 mm. Hg. Two of these pa-

tients had pupillary membrane with iris bombé and the third had had elevated tension for a considerable period of time. These patients differed in no other way, however, from the other 10.

Two elderly women of this series developed agitation and confusion following the administration of urea. One of these two patients inadvertently received almost two gm. of urea per kg. of body weight. Both patients returned to a normal mental status following a night of sleep. All other side-effects were mild.

Gonioscopy following lowering of tension by urea revealed that the angle remained closed despite lowering of tension. Hence it may be assumed that urea acts independently of the state of the angle of the anterior chamber.

Hemorrhagic diabetic retinopathy treated by hypophyseal stalk section

Joel S. Contreras, M.D., Richard A. Field, M.D., W. A. Hall, M.D., and W. H. Sweet, M.D., presented case reports on three patients with hemorrhagic retinopathy due to diabetes mellitus in whom favorable effects on the retinopathy were seen after hypophyseal stalk section. In each patient preoperative visual acuity was recorded, slitlamp examination of the anterior segment was performed, and drawings, which were actual mappings of every vessel aneurysm and hemorrhage, were made. Aneurysms and hemorrhage were related to vascular pattern. Thus location and size of these abnormalities could be accurately followed in relation to the vascular pattern. Photographs of the pre- and postoperative fundus drawings of each patient were presented and discussed.

Postoperative examination in all three patients revealed a dramatic cessation of hemorrhage. Blood absorption was enhanced and proliferation of tissue underneath hemorrhage was prevented. Blood flow within the vessels was improved. Neovascularization was strikingly affected. Racemose aneurysms remained the same but they underwent a shrinking phenomenon. Exudates showed a tendency to slow migration both vertically and horizontally but the exudates themselves have not disappeared. Disappearance of abnormal vitreous turbidity occurred within a few days after the operation.

Migrainoid symptoms with cerebral anomalies

Robert Reinecke, M.D., reported a case of migrainoid symptoms with certain unusual features. Its pattern of headaches was unusual in that it was always limited to the distribution of the second division of the left trigeminal nerve. A parieto-occipital arteriovenous abnormality was demonstrated which could account for the visual aura. Two aneurysms were demonstrated and a third postulated to explain the salient features of this case.

The patient was a 43-year-old woman who had had recurrent headaches since the age of 15 years which were preceded by a right visual field aura. Three weeks prior to admission she had developed almost daily headaches. She developed a stiff neck nine days prior to admission and vertigo, diplopia and left ptosis developed. On physical examination the left eye showed ptosis, dilation of pupil, and deviation outward, with retention of intorsion. On lumbar puncture the spinal fluid was orange and showed 60,000 red cells per c.mm. Arteriogram showed a balloon-type aneurysm at the origin of the right posterior communicating artery. This aneurysm, however, does not explain the patient's left third nerve palsy and left cephalalgia. A left arteriogram showed an arteriovenous abnormality in the left parietal occipital area. It is necessary to postulate a third aneurysm of the left posterior communicating artery to explain the third cranial nerve palsy on the left and the cephalalgia. This was not demonstrated on the arteriogram. It is assumed that a clot in this anuerysm prevented demonstration by arteriography.

Despite the demonstration of organic

causes of this patient's migraine type disturbances, it is necessary to postulate idiopathic features to explain the periodicity. This case demonstrates that migraine symptoms might mask pathologic intracranial changes until overt intracranial bleeding occurs. A constant visual or trigeminal cephalalgia may be sufficient cause for a complete neurosurgical work up.

Diagnosis of orbital lesions

Ira S. Jones, M.D., discussed the diagnosis of orbital lesions and said this is primarily a discussion of unilateral exophthalmos.

Recognition of exophthalmos can sometimes be difficult. False readings with the Hertel exophthalmometer are common. A better idea of the presence of exophthalmos and its degree can be obtained by having the patient bend his head forward and sighting down the forehead toward the cornea of each eye. It is possible to confuse enophthalmos on one side for exophthalmos on the other. Retraction of the upper lid can also give the appearance of exophthalmos.

Paralysis of the extraocular muscles may lead to two mm. or more of exophthalmos. Asymmetry of the skull or orbits may give a true exophthalmos without disease. A large globe may give a false impression of exophthalmos.

History, inspection, auscultation, study of ocular motility, and palpation are indicated in each patient with exophthalmos in order to make proper differential diagnosis. General medical examination should follow. Infiltrative exophthalmos due to old thyroid disease may appear many years after a history of thyroid disease. The Werner provocative test is useful in differentiating thyroid exophthalmos from exophthalmos of other causes.

On palpation of the orbit the patient should be asked to look in the direction in which you are palpating. If, for example, the patient looks upward while you are palpating below, the orbital septum is placed under tension and a false idea of mass is obtained. If the patient looks down while the lower orbit is palpated the septum is relaxed and a truer idea of the contents of the orbit can be obtained.

When a mass lies in the muscle cone, there are frequently striae in the posterior portion of the retina. If striae occur more anteriorly, they are not as helpful in establishing the presence of a mass within the muscle cone.

In a recent analysis of 100 X-ray films of patients with exophthalmos, 80 percent had abnormal findings. Usual X-ray examination includes the skull, orbits and optic canals. Stereoscopic X-ray films are preferred. X-ray findings are calcifications within the orbit, differences in appearances between the two orbits, changes in shape of the orbit, compression of bone from erosion and fracture, enlargement of the optic canal, and increased bone density. All other changes are combinations of these six changes.

In cases in which the diagnosis is in doubt following the diagnostic procedures outlined herein, exploration of the orbit is carried out. Photographs and radiographs of a number of different patients with different causes of exophthalmos were presented. The Krönlein operation with modifications is the operation of choice for exploration of the orbit and removal of orbital tumors.

A technique of exenteration with temporalis graft into the orbit was described. In a series of 230 cases with unilateral exophthalmos, thyroid disease was the most frequent cause. Hemangiomas, lymphomas, granulomas, lacrimal gland tumors and meningiomas followed in decreasing frequency as the causes of unilateral exophthalmos.

Dr. Virgil Casten followed this presentation with a description of surgical techniques in the management of orbital tumors, illustrated by a large number of representative cases.

Robert J. Herm,
Recorder.

AMERICAN JOURNAL OF OPHTHALMOLOGY

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NATIONAL MEDICAL FOUNDATION FOR EYE CARE*

FIFTH ANNUAL REPORT OF THE PRESIDENT

Five years have passed since that day in October, 1956, when some 600 of us met in this hotel and wrote our names on slips of paper, thus signifying our intention to become charter members of a new ophthalmological organization. Out of this was born the National Medical Foundation for Eye Care.

The original membership of 600 has now grown to more than 2,500. Nearly four million pieces of literature have gone out to the

* Text of address prepared by Ralph O. Rychener, M.D., president of the National Medical Foundation for Eye Care and presented at an open meeting of the Foundation at the Palmer House, Chicago, October 8, 1961.

people of this country over the Foundation's signature.

The Foundation, its publications and other activities have been mentioned and quoted throughout the country and far beyond in press, magazines, television and radio. The central office handles each year thousands of letters and calls from all over the world on all aspects of eye care.

Working on this project from day to day, I have often been overwhelmed and sometimes frustrated, at the tremendous variety of challenges, problems and concerns which have come to this Foundation.

On the other hand, it sometimes comes as a surprise to me, reviewing the five-year span since we were organized, to realize the tremendous progress we have made and the enormous amount of work we have accomplished. I feel that all of us who have had some part in organizing, working for or supporting this Foundation may well take pride in what it has done in its first five years.

Right at the start, it seems to me that this report should mention a milestone in ophthalmology's efforts to clarify the relationship of medicine to optometry. I refer to the adoption by the American Medical Association of the report of its Subcommittee to Study the Relation of Medicine to Optometry.

This report provides a solid basis, heretofore lacking, for ophthalmology in formulating its own policies. And this new base, from which we can operate with secure confidence, is founded in the body of American medicine, enunciated by the American Medical Association. It clearly states the position of medicine on the subject of eye care. As most of us will recognize, this is a statement that has been needed, not only by ophthalmology but by American medicine for the past 25 years.

Let me emphasize that this is an A.M.A. action, and not a product of the National Medical Foundation for Eye Care. But I may say that this report would probably never have been drafted, much less adopted, without an active, determined National Medical Foundation for Eye Care which had probed and expounded the informational basis on which this report rests. I would like to express on behalf of the Foundation, and I am sure for all ophthalmologists, our thanks to three members of the A.M.A. Subcommittee which prepared this report, who are also devoted members of the Foundation: Drs. Harold F. Falls, Chairman of the Executive Committee of the Foundation, Charles E. Jaeckle, Secretary-Treasurer of the Foundation, and Barnet R. Sakler, our Vice-President.

A summary of the report itself has been presented in the August *News Bulletin* of the Foundation, and a complete version of the report, together with an editorial on the subject, will appear in an early issue of *J.A.M.A.*

I urge you to pick up a copy, read it and study it yourself and then get some extra copies for your medical colleagues, your local newspapers, legislators and any others who need to be informed about the meaning of medical eye care and the difference between such care and other services offered in the eye field.

During the past year the Foundation completed a project which has long needed doing; an exposé of the widely circulated optometrically sponsored pamphlet titled, "What Medical Authorities Say About Drops." This unfortunate bit of propaganda should long ago have been repudiated and disavowed by optometry itself. It served no useful purpose except to raise unfounded questions in the minds of patients as to the use of cycloplegics in eye examinations. It contributed nothing to the public welfare except confusion.

The Foundation investigated this pamphlet. We discovered that the so-called "medical authorities" quoted in this publication had very little claim indeed to being medical authorities. We discovered that these persons had, in some instances, been completely

misquoted, and in other instances their intended meanings had been distorted by being lifted out of context or otherwise edited. In short, this pamphlet is a tissue of falsehoods. We believe we have exposed it thoroughly and we ask that you continue with the exposure, so that its unfortunate effects can be thoroughly obliterated. You have received copies of this report and more copies are available at the Foundation's exhibit here.

It should not be necessary for me to point out the uses to which this report can be put. Not only does it serve to clarify the confusion about the use of drops, but also to indicate the purposeful source of some of this confusion. The response of the medical and public press to this material proves it to be timely and of general interest.

While we are on the subject of publications, may I call your attention to several new pieces published by the Foundation, including our attractive little booklet for glaucoma patients titled, "Living With Glaucoma" and our extremely popular pamphlet on the eye care of children titled, "Eye Cues for Eye Care." Please notice, also, the new format of all of our Foundation publications for the public. They have been brightened up and made more lively and eye-catching. We hope this investment will be returned to us in greater readership and more effective service to the public.

I think it is scarcely necessary to remark upon our outstanding *News Bulletin*, which has been enthusiastically received by ophthalmologists and also by the medical press generally.

The 1961 survey of state legislation affecting eye care appearing in a recent *News Bulletin* was most valuable to many of us involved in state legislative problems.

This year the Foundation has conferred its First Annual Helmholtz Award on Mr. John Kord Lagemann, author of an article titled, "The Facts About Your Eyes," which appeared in *Redbook Magazine* in May, 1960. Mr. Lagemann's article was adjudged by our distinguished Advisory Board as the best article on any aspect of eye disease and eye care published in a popular magazine during the preceding 12-month period. We believe this annual award will prove a useful stimulus toward better writing in the field of eye care for the people.

Our committees are hard at work on several projects. The School Eye Health Committee has been very active. Among other things, it prepared the pamphlet, "Eye Cues for Eye Care," and it is working on other projects to help parents, teachers, school physicians, nurses and supervisors.

The Contact Lens Committee now has in hand the results of a nationwide survey made by the Foundation to determine just how ophthalmologists are handling the examination, prescription, fitting, and after care of contact lens patients, and the results of the various procedures used.

The Committee on the American Registry of Ophthalmic Technicians is now hard at work upon data collected by the Foundation from ophthalmologists throughout the country. This material indicates the pattern of employment and use of ophthalmic technicians by ophthalmologists: how many of them there are, what functions they perform, and so forth. The raw data has been processed by computers and is now being interpreted by our Committee. The results of this type of Foundation committee work and research will, undoubtedly, have a profound, far-reaching effect upon the practice of ophthalmology in the future. We are gathering, organizing, analyzing and interpreting information for the first time which will, when complete, accurately indicate national patterns of practice, trends in the modern evolution of ophthalmology, as well as our strengths and weaknesses. Most important of all, it will indicate what needs to be done and how to go about doing it most effectively.

In this connection, I would like to call your particular attention to the extremely valuable and informative paper on the "Op-

portunities and Problems Confronting Ophthalmology in the Sixties," which was presented by Dr. Frank W. Newell of Chicago at the special conference of ophthalmologists held in New York City on June 26th. This paper was extensively reviewed in our *News Bulletin* for September and it deserves a careful reading and re-reading by every one of us.

Perhaps you will forgive my enthusiasm, but I would like to express the opinion that if the Foundation had done nothing more than initiate its several surveys and studies in the areas of ophthalmological practice already mentioned, its existence would have been more than justified. We are now beginning to establish for the first time a factual picture of just what is going on in the practice of ophthalmology in America. Heretofore we have had to rely on individual subjective impressions to a very large extent. The value of such studies in better informing our policies in the future could scarcely be exaggerated.

As the Foundation continues to earn respect and recognition as an effective voice for American ophthalmology, it will be able to present the views of ophthalmology with greater impact.

In New York City last June some of your Foundation officers met with representatives of the National Society for the Prevention of Blindness, the better to co-ordinate our respective activities. Basically we are trying to eliminate confusion and misunderstanding in presenting the story of medical eye care to the people, to obviate overlapping or duplication of effort, and to achieve for the work of both organizations maximum effectiveness.

I am delighted to report that the representatives of the National Society for the Prevention of Blindness were most receptive and responsive to the ideas which we proposed and the suggestions we offered. I can assure you the Society welcomes the views of the practicing ophthalmologist, and on your behalf the Foundation welcomes the opportunity to co-operate with the Society. This exchange of views has been placed on a continuing basis and your officers are meeting with the representatives of the Society again this week to discuss other matters of mutual interest.

We have been active with other organizations in our field. By the action of the Foundation ophthalmology was officially represented by the chairman of our School Health Committee at the National Conference on School Health jointly sponsored by A.M.A. and the American Education Association. We were officially represented, too, at both of the recent White House conferences, namely, on ageing, and on children and youth. The Foundation's representatives were the only spokesmen for ophthalmology at these three conferences. We are to be represented on a committee organized by the American Medical Association to develop a plan for emergency medical indentification of persons having special sensitivities or chronic conditions, such as glaucoma and diabetes. We are also an active member of the National Committee for Research in Ophthalmology and Blindness.

The Foundation has for several years been recognized by the American Medical Association as an authoritative source of information and advice in the socio-economic and public information areas of eye care.

In connection with our expose of "What Medical Authorities Say About Drops" it may be useful to call your attention to the apparently developing confusion in optometry, evident in a recent inconsistency of policy and attitude toward the use of drugs in diagnosis and treatment of eye conditions.

While optometry, on the one hand, attempts to convey the impression that drops are not necessary to an examination of the eye (which, of course, is the burden of their misleading pamphlet), on the other hand they seek to force through legislation, most notably and recently in Pennsylvania, which would have enabled them to use medication. The question confronting optometry today

seems to be: to use drops or not to use drops?

This confusion and contention within optometry over the use of medication is but a manifestation of a deep, basic and bitter schism over the fundamental issue: Will optometrists stick to the practice of refraction, or will they attempt to become eye physicians by legal fiat?

From personal knowledge we can testify that this question is producing serious and growing contention in the optometric ranks. Many optometrists are determined to remain within the bounds of their competent training. Some of these are increasingly annoyed at the determination of some of the more aggressive leaders to convert optometry into medicine by legislation and high-powered lobbying, such as they attempted, unsuccessfully, this year. It is interesting to note that the Pennsylvania expansionists were reprimanded by the national body for their abortive putsch into the practice of medicine, but one can scarcely avoid noting that there was no repudiation of the effort while it was in progress.

In years past, when the Foundation was in its early infancy, I usually found it necessary to devote some major part of my annual report to a fervent appeal for more members—just to provide us with the minimum funds with which to carry on. Today —although we need every cent we can get from our loyal members merely to carry on our basic programs—nevertheless, I would prefer to base this appeal for universal membership of American ophthalmology on the need of the Foundation to complete its internal organization and to become a truly representative and authoritative voice for our profession. As the members of our Board of Trustees declared in our current *News Bulletin,* in their special message to the members of the Foundation, this Foundation: "cannot represent *you*—its policies cannot truly reflect *your* wishes and judgment—unless *you* are part of the Foundation. The present membership of the Foundation is representative of our profession as a whole. But if *you* are not a member, you deprive yourself of a national channel for expression of your views.

"If *you* are *not* a member of the Foundation, isn't it high time to join? If *you* are a member, isn't it high time to see to it that all your colleagues put *their* shoulders to the wheel?

"We believe the time has come for every ophthalmologist to contribute his share of support and to add his voice to this increasingly articulate and respected voice of American ophthalmology.

"The time for action is NOW."

Ralph O. Rychener.

A DECLARATION OF MEDICAL PRINCIPLE

When "refracting opticians" first became licensed as optometrists, they made no pretense to any functions (beyond the optician's traditional role of providing and fitting spectacles) other than determining, without the use of drugs, the manner in which an eye focused light and what lenses would compensate for the refractive error to produce a focused image in that eye. By definition the "practice of optometry" as a licensed occupation* included the use of any means other than the use of drugs to accomplish this specific purpose. These functions were then also performed, and continue to be performed by physicians providing medical care for all conditions of the visual system—physicians who not only use drugs when appropriate in refraction but whose concern has encompassed and whose responsibility extends to every aspect of the patient's welfare relative to vision and the eye.

From the beginning the optometrist was distinguished from the physician by a limited authority and responsibility in refrac-

* Contrast the use of the word "optometry" as a medical term, originated a quarter century earlier: the measurement of the refraction of the eye.

tion, and no authority or responsibility for anything else. By the exclusion of the use of drugs, the optometrist was limited to only a part of refraction, itself only one area of ophthalmology, a branch of medicine. Not only did the legislatures—with the wholehearted consent of the optometrist—seek to make this clear by the specific exclusion of the use of all drugs by the optometrist but, in a number of instances, the law stated that nothing in the act should be construed as authorizing the use of any form of treatment other than spectacles, or as authorizing the diagnosis of disease, or as authorizing the designation of an optometrist by the term "eye specialist."

The optometrist did not regard or represent himself as an "eye doctor," "eye specialist," or "vision specialist." When the terms "eyesight testing" and "eyesight specialist" were sometimes used they were understood by the public—and intended by the optometrist—to refer specifically and exclusively to refractive procedures.

In recognition of this sharp limitation of the optometrist, the law sharply discriminated between the optometrist and the physician in the educational qualifications demanded. The relation of medicine to optometry was then unmistakably clear. The optometrist invited only those who sought correction of refractive error by glasses. The state having discriminated between optometrist and physician as to educational requirements, there was no suggestion that the public or the state should thereafter fail to discriminate.

When he sought licensure, the optometrist neither contended nor believed that he was qualified to determine whether disease was present or not present, or to advise as to the need for medical or surgical examination or treatment, or to evaluate any condition of the visual system other than the refraction. Nor did the people have any illusion that he was so qualified. The optometrist's claim for public acceptance was based on the premise that, for at least a considerable number of people, refractive error could be adequately determined by someone without the training of a physician and without using drugs.

It was argued that since the optometrist's training was decidedly briefer, simpler and less costly than that of the physician, his services as refractionist could be supplied at a lesser cost than those of the physician as examiner-refractionist. It was acknowledged that the care of a patient with disease of the eye was within the province of the physician alone.

It was suggested, however, that the presence of eye "disease" would sometimes be evident to a person without a physician's training and, if the optometrist on occasion observed evidence of disease, he would have no hesitation in advising that a physician be consulted. If a person with a red eye did not himself recognize that he needed a physician, would not any optometrist whom he consulted enlighten him?

Under such circumstances optometry became a legally identified vocation. Under such circumstances Columbia University in 1910 established a course in optometry, since discontinued. When the A.M.A. House of Delegates in 1959 ordered the study of the relation of medicine to optometry, it noted that in the intervening years widespread public confusion had developed.

The A.M.A. Judicial Council pointed out to the House of Delegates in 1951 that there was a natural tendency of all groups functioning either on the periphery of medicine or within a small part of the field of medicine to extend the scope of their activities. It is understandable that optometrists concluded that, if they possessed some knowledge of diseases of the eye, they could be more helpful to those who consulted them. The objective was not to qualify the optometrist to "diagnose disease," but to qualify him to "recognize the abnormal" when he saw it. In course, it was proposed that the optometrist look for the abnormal.

Having taken the position that he should be qualified to "recognize" the abnormal

when he saw it and that he should look for it, it was a logical step for him next to conclude that he would detect the abnormal if it were present, and conversely could determine when the abnormal is not present. Is it surprising that sometimes, having concluded that he possessed this competence, the optometrist next concluded that he was competent to determine whether a given condition required medical treatment? Many optometrists assume these functions of the physician.

If such thinking seems quite specious and illogical to the physican, let him remember that the understanding of disease and health which he possesses is acquired only with a medical education and training.

Absent from the optometrist's thinking was comprehension that diagnosis is the most difficult branch of medicine, and that the "recognition of the abnormal" or "detection of disease" are parts of the diagnostic process; that diagnosis of the absence of disease is the most difficult diagnosis the physician is ever called upon to make; and that diagnosis is a continuing process, requiring the total training of the physician.

Statements by individual optometrists, optometric literature, official optometric pronouncements indicate that many optometrists adhere to the idea that the optometrist is competent to decide whether medical treatment is called for, and by which branch of medicine, and to the idea that the ophthalmologist's function is primarily and essentially surgical.

Optometrists should understand the fallacy of these tenets, however sincerely they have been taught, and however sincerely the optometrist has sought to apply them. Diagnosis has been delayed and the optometrist has repeatedly been embarrassed by his adherence to them. The injury patients have suffered from such delay in diagnosis is not due to an optometrist's human error. To human error we all are subject, and the optometrist differs not from the physician or any other man. The harm comes not from failure of the optometrist to exercise his competence but from his attempting to assume functions of the physician without the physician's training. The unqualified observer may look and not see; search, but not know for what to search; observe, but not have the knowledge to interpret. He cannot always know when a physician is needed.

Optometrists do sometimes note ob[illegible]us deviations from the normal. On some occasions they inform the individual that there exists a condition the evaluation of which demands the competence of a physician. Sometimes they do not and, as a result, diagnosis is needlessly delayed. When as a consequence an eye is lost, is the optometrist accountable or does the onus rest on the system?

When an optometrist on the faculty of an optometric school, working in the school clinic, gives orthoptic training to a child with brain tumor, whose disease was at that time unquestionably diagnosable by a physician, it is not the optometrist that is responsible but the system. When the differential diagnosis is between presbyopia and glaucoma, the majority of patients will be found to have only presbyopia. A patient with glaucoma may procure entirely satisfactory glasses from an optometrist. When his glaucoma, which could have been diagnosed early had he been seen by a physician, is diagnosed late, there is small comfort for the patient in the knowledge that he is in the minority. Again it is not the practitioner but the system which is inadequate. When, contrary to fact, an optometrist has asserted, "there is no disease," or, "you do not have glaucoma," society will ultimately pay the cost of any resulting permanent impairment. What recourse has the patient?

Examination and diagnosis are the essence of the practice of medicine. "Certainly the training to be required of one who would hold himself out to the public as competent to give a qualified opinion about the eye and the visual system, . . . the second to seventh cranial nerves and their associated pathways

in the brain . . . can not be less than that required to qualify (him) to enter upon the practice of medicine."* There can be no justification for singling out the patient with ocular complaints for management by one with less training than the physician's. This is the issue between Medicine and Optometry.

The optometrist is never a substitute for a physician.

The optometrist is engaged in a field which is not apart from medicine but he has affirmed his desire to be an independent practitioner. No simple test may be applied to establish that the need is for refraction and glasses alone. The symptoms of serious disease may be mistaken for signs of simple defect correctible by glasses.

The solution does not lie in teaching the optometrist a little medicine, or in his practicing a little medicine. In "Medical Care For Eye Patients,"† the medical profession has made a declaration of principle, providing a basis for definition of existing problems. It is conceivable that the medical profession can contribute to a different orientation of the optometrist with benefit to the public and to the optometrist.

Charles E. Jaeckle.

* Editorial "What is the issue?" Am. J. Ophth., *51*:718 (Apr.) 1961.

† Report of the A.M.A. Subcommittee to Study the Relation of Medicine to Optometry, approved by the House of Delegates, June 29, 1961.

CORRESPONDENCE

South American ophthalmology

Editor
American Journal of Ophthalmology:

Regarding the article on "South American ophthalmology" by C. Dwight Townes, M.D., and Arthur H. Keeney, M.D., which appeared in the July, 1961, issue of The Journal, I could not keep silent about our hospital.

Sixty miles from the capital of São Paulo, in a city of 200,000 people, Campinas, there is an entirely private hospital for ophthalmic patients with 175 beds. The staff has 15 ophthalmologists, six otolaryngologists, two orthopedists, three anesthesiologists, four laboratory doctors, two radiologists, one cardiologist and two dentists, all working full-time. Last year, there were 30,493 eye consultations, 2,361 major eye operations and 392 minor eye operations. Staff meetings are held every other week and the most interesting papers are published in our *Arquivos do Instituto Penido Burnier*.

(Signed) Aloysio Alfonso Ferreira, M.D.,
Campinas, Brazil.

Patients on Equanil and Meprobamate

Editor
American Journal of Ophthalmology:

I should like to call the attention of The Journal readers to the fact that not infrequently patients on Equanil and Meprobamate have found that they have a loss of visual acuity for near objects. This occurs predominantly in individuals under the age of presbyopia and will last as long as these drugs are used.

Two additional ocular findings, less frequent and more usually occurring in the older age group are (1) partial or complete loss of pupillary reaction to both light and convergence and (2) convergence insufficiency. We have found that 48 hours after the drugs have been stopped there is a recovery of loss of accommodation to the normal.

I am sure it is well known that patients taking belladonna by mouth and diethylstilbesterol by injection and also others on large doses of bromide will have a partial or complete paralysis of accommodation. My reason for reporting all of this is because of the indiscriminate use of the Equanil and Meprobamate in the past years.

(Signed) Leo L. Mayer, M.D.,
Jackson, Mississippi.

BOOK REVIEWS

TRAITEMENT CHIRURGICAL DES AFFECTIONS OCULAIRES: VOLUME II. By L. Guillaumat, L. Paufique, R. de Saint-Martin, S. Schiff-Wertheimer and G. Sourdille. Paris, G. Doin et Cie. 607 pages, 285 illustrations and index. Price: 145 NF (about $29.00)

This is the second volume of a projected three on ocular surgery by an illustrious group of French ophthalmologists. Volume I appeared in 1957 and received an excellent press in its native France and in this country. Volume II concerns itself with surgery of the conjunctiva, cornea, lids and lacrimal passages. Unhappily, two of the contributors, Drs. Sourdille and Schiff-Wertheimer have died in the intervening years. The remaining authors have continued the plan of the first volume in describing surgical techniques most commonly used by them and giving full coverage to complications of these procedures and their treatment.

Diseases of the cornea and corneal transplantation have long been a specialty of French ophthalmology and accordingly these receive detailed coverage in this volume. Largely, the techniques described are those in use in this country. There are some differences in other areas, however. For example, the preferred treatment for small epitheliomas appears to be radiation while most American ophthalmologists prefer wide excision. On the other hand, chalazia are apparently usually excised in toto while simple incision and curettage is condemned. These differences are minor and over all this in an excellent volume and the simple line drawings that profusely illustrate the text make a profound knowledge of French unnecessary.

David Shoch.

TRAITEMENT CHIRURGICAL DES AFFECTIONS OCULAIRES: VOLUME III. By L. Guillaumat, L. Paufique, R. De Saint-Martin, the late Mme. S. Schiff-Wertheimer and G. Sourdille. Paris, France, G. Doin and Company, 1961. 423 pages, 320 illustrations, including 163 in color, index.

Volume III of this well-known textbook and atlas of ocular surgery concludes this series. It contains descriptions of the surgery for strabismus, retinal separation, ocular tumors, ocular and orbital prostheses and diseases of the orbit.

Volume I appeared in 1957 and covered the subjects of surgical principles, cataract, glaucoma, iridocyclitis and ocular trauma. An addendum to Volume I now appears. Its subject is the extraction of cataract with alpha chymotrypsin. The authors wisely favor its conservative use.

Those who read French will enjoy this volume, as they have the others. Non-French-reading ophthalmic surgeons will profit by a careful study of the excellent illustrations and be able to follow fairly well the arguments pertaining to them.

The work is well designed and extraordinarily well edited into a coherent and lucid text. This is a remarkable achievement considering the number of eminent collaborators involved, each with his own ideas on "how to do it." It is unnecessary to say that their ideas are indeed first class.

The opening chapter on the surgery of strabismus particularly interests us. It is only recently that the French ophthalmic surgeons have become "steamed up," so to speak, over this subject. This late development of keen interest in ocular muscle surgery is difficult to understand in view of the fact that many early French ophthalmologists, such as Javal, Parinaud, Rémy, Cantonnet, Ronfray, were pioneers in the study and treatment of strabismus.

The authors say that "thanks especially to the efforts of Edward Hartmann, modern conceptions of treatment are accepted by most of the ophthalmologists." The influence of the modern Anglo-Saxon "muscle men," especially the Americans, upon our French colleagues has been very great. It is not too devious to trace the skillful hand of

Conrad Berens through the actions of Edward Hartmann who spent many years with Berens in New York and returned to France indoctrinated and convinced, as an apostle of the new knowledge in this subject. This is pleasing indeed to us here, for it represents a small payment of the debt we all owe to European (and British) ophthalmology over the years, and particularly to the French who have given us so very much.

The three volumes of this textbook are excellent and one is indeed proud to add them to his shelf of books pertaining to ocular surgery.

Derrick Vail.

NEURO-ENDOCRINE ASPECTS OF OPHTHALMOLOGY. By M. Radnót. Budapest, Verlag der ungarischen Akademie der Wissenshaften (Akadémiai Kiadó), 1961. In German, 238 pages, 115 illustrations, some in color. Price: etwa $8.00.

M. Radnót has devoted 20 years of research to neuroendocrine aspects of ophthalmology. Numerous references to original papers attest her activities in this field. These initial statements are made to emphasize that some of the author's conclusions may appear farcical at first glance but should not be glossed over or dismissed as utter nonsense. Perhaps some of these conclusions might sound more convincing after a perusal of the original articles. Someone interested in the subject might be tempted to duplicate some of the observations reported.

In the first five chapters, Radnót considers endocrine disturbances of the lids, the conjunctiva and cornea, the sclera, the uvea and the lens. There is little doubt that some forms of keratitis sicca result from endocrine disturbances. Yet one wonders about the significance of an observation by Gáll according to which the contralateral testis or ovary is either missing or disturbed in cases of unilateral keratitis sicca. A report by Imre of three cases and one by Arques of one case on the development of keratitis sicca after cataract surgery, as well as a report by Larmande on the improvement of an existing keratitis sicca after lens extraction, seems to be less proof of a causal relationship than of the fact that statistics can be twisted to fit any conclusion if they are based on a sufficiently small series. Similarly, the idea of a "pluriglandular" etiology of keratoconus seems to be highly questionable, particularly in view of the hereditary tendency of this anomaly postulated in the following paragraph.

The influence of endocrine disturbances on the uveal system and the lens are treated in a rather perfunctory manner. The description of the ocular findings may be adequate enough for the nonophthalmologist, but the ophthalmologist interested in a detailed presentation of the physiopathologic and clinical aspects of most of the entities in question will find these chapters disappointing.

The chapter on the various forms of retinopathies, in general leaves little to be desired. However, it would seem to be objectionable to consider the pigment degeneration of the retina as an endocrine disturbance. Even the Laurence-Moon-Biedle syndrome, a well-defined entity which must be differentiated from the classic form of pigment degeneration of the retina, is a heredofamilial form of disease with signs only suggesting an endocrine disturbance. It also seems to be far fetched to consider Eales' disease an endocrine disturbance for the reason that it occurs predominantly in young supposedly healthy men, whereas women showing the disease have "endocrine disturbances," and because a spontaneous improvement has been observed during pregnancy.

The most satisfying chapter is the one dealing with the endocrine exophthalmos. Radnót does not follow Mulvany's concepts but prefers to distinguish a "compensated" from a from a "decompensated" exophthalmos, a belief shared by an increasing number of ophthalmologists in this country. The presenta-

tion of the entire subject is thoroughly up to date and quite exhaustive.

The most controversial chapter seems to be the one dealing with the influence of endocrine disturbances on the intracular pressure. Perhaps it is unfair to quote some of the author's conclusions out of context; nevertheless, these conclusions are quite startling. Radnót was able to reduce the intraocular pressure in a rabbit eye by removing the testicle on the contralateral side. X-ray radiation and ligation of the vas deferens had the same result. Removal of the ovaria had a similar effect. However, uterus extirpation, with the ovaria left intact, was followed by an increase in the intraocular pressure. It must be emphasized in all fairness that the author does not advocate such procedures as the method of choice in the treatment of glaucoma, although she quotes Tschemolossow who employed a ligation of the vas deferens, with only temporary success. Obviously the patient had bilateral glaucoma because Radnót states that no unilateral ligation was used. It seems that she regrets only that this made it impossible to determine whether unilateral ligation in man also affects only the contralateral eye.

Ophthalmologists should not despair, however, that the treatment of glaucoma might be taken over eventually by the urologists. It may well be possible that the treatment of impotence henceforth will be the domain of the ophthalmologist. Radnót was able to observe that exposure of one eye to light results in hypertrophy of the testicle or ovary on the contralateral side. So far her experimental studies have been limited to birds, mostly ducks and chickens. But she quotes an observation by Marx that impotence occurred in soldiers stationed in the northern parts of Norway which disappeared after their return to southern regions.

In all seriousness, the chapter on the importance of the eyes for the function of the endocrine organs is quite thought provoking. It is impossible to mention in detail the various investigations the author has undertaken. All conclusions are well documented by numerous macroscopic and microscopic illustrations, as well as by a large number of curves. These conclusions certainly could not be refuted by logical reasoning but would have to be proven or disproven by repeating these investigations and by comparing and evaluating the results.

In summary, this volume is not the ideal textbook for the clinician in search of information on endocrine disturbances affecting the eye. The thoughts expressed may sound startling but cannot be simply dismissed as unscientific. The author supported most of her contentions by extensive research.

Each chapter is appended by an adequate bibliography. The illustrations are well chosen and beautifully reproduced.

Stefan Van Wien.

SPACE AND SIGHT. By M. von Senden. (Translated from the German by Peter Heath.) Glencoe, Illinois, The Free Press, 1960. 338 pages, select bibliography (B. R. Singer), index. Price: $10.00.

"Suppose a man born blind and now adult, and taught by his touch to distinguish between a cube and a sphere of the same metal, and nighly of the same bigness, so as to tell when he felt one and the other, which is the cube, which the sphere. Suppose then the cube and the sphere placed on a table, and the blind man made to see: quaere, 'whether by his sight, before he touched them he could now distinguish and tell which is the globe, which the cube?', to which the acute and judicious proposer answers not.

". . . I agree with this thinking gentleman whom I am proud to call my friend, in his answer to this his problem; and am of the opinion that the blind man, at first sight, would not be able with certainty to say, which was the globe, which the cube, whilst he only saw them; though he could unerringly name them by his touch, and cer-

tainly distinguish them by the difference of their figures felt." (John Locke, *An Essay Concerning Human Understanding*, 1690, Bk. II, Chapter IX, Section 8.)

Two hundred and seventy years later, Dr. M. von Senden in a most scholarly fashion dissects and discusses the matter of perception of space and shape in congenitally blind patients, before and after operation. It is a fascinating book.

Derrick Vail.

THE STORY OF DISSECTION. By Jack Kevorkian. New York, the Philosophical Library, 1959. 79 pages, 16 illustrations (portraits), references. Price: $3.75.

This is a most interesting account of dissection of the human body from antiquity to the present. The early history is fog-bound in the mist of superstition, religion and repugnance, as one would expect. What fragments remain of the earliest times are too scanty to be of help. Forensic pathology undoubtedly was practiced to a small degree in those remote days. As the centuries unfold, the pace quickens, halted here and there as religion and superstition gain the upper hand, and speeded up by the work of sporadic geniuses who were not deterred by the more or less unfavorable environment in which they worked. This is graphically illustrated at the end of the book, where the line of progress looks like an electrocardiograph. It is fascinating reading.

Derrick Vail.

THE BLIND PERSON AS A COLLEGE TEACHER. By W. A. McCauley. New York, American Foundation for the Blind, 1961. 88 pages, paperbound. Price: $1.00.

Among 189 colleges having blind students, 103 have two or more such students. A few schools will not admit blind students; most of these are teacher's colleges, technical schools, or institutions controlled by religious orders training men for the priesthood. Seventy-four colleges and universities reported having one or more blind teachers on their faculties. In assessing the potential of blind persons for college teaching careers the author was assisted by five totally blind professors. The motivations underlying the decisions of blind students to enter college teaching are not different from those of sighted persons. The blind teacher must be prepared to pay for some help in the performance of his duties; the average expenditure amounts to about $500 annually. The blind teacher contributes, produces and competes on the same basis as his colleagues, and participates to the same extent in civic and professional organizations.

James E. Lebensohn.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

9

GLAUCOMA AND OCULAR TENSION

Diaz-Dominguez, D. **Relationship between high myopia and ocular hypertension.** Ann. d'ocul. 194:597-606, July, 1961.

Tonometry and tonography were performed on 144 eyes with a myopia greater than 10 diopters. The average tension was 17.83 mm. but in a fourth of the patients the tension was over 21 mm. The average value for a facility of outflow was 0.14 but in a third of the eyes values below 0.09 were obtained. The author does not feel that this necessarily indicates that ocular hypertension causes a lengthening of the globe but rather that the abnormal growth of the globe causes a reduction in the facility of outflow with a subsequent increase in intraocular pressure. He advises that in all patients with myopia over nine diopters, careful tonometry and perimetry be performed. In these cases particular attention must be paid to variations in scleral rigidity. (21 references) David Shoch.

Galin, M., Nano, H. and Baras, I. **The suction cup method in the early diagnosis of glaucoma.** Rev. brasil. oftal. 20:177-183, June, 1961.

The authors feels that tonography is a cumbersome procedure, frequently limited to teaching hospitals and describe another method to measure the facility of outflow which does not require a large amount of costly equipment. After the intraocular pressure of a patient has been checked, a special suction cup is placed over the sclera and connected to a mercury manometer. A certain amount of vacuum is created which theoretically should close off the episcleral veins, so that outflow is impeded while normal aqueous production continues. After 15 minutes the suction cup is removed and the pressure is taken again. After another 15 minutes the pressure is checked once more and from tables it can be calculated how effective the drainage has been. If the pressure has not returned to normal 15 minutes after the removal of the suction cup, there is a definite obstacle to the flow of aqueous. For daily practice, instead of making cumbersome calculations, it suffices to know that if the pressure is not back to normal at the time of the last reading we are dealing with a glaucomatous patient. (2 figures, 3 tables, 14 references) Walter Mayer.

Gloster, J. **Influence of the facial nerve on intraocular pressure.** Brit. J. Ophth. **45**:259-279, April, 1961.

Stimulation of the facial nerve in cats and rabbits led to a rise in intraocular pressure. Stimulation of the greater superficial petrosal nerve, which carries many parasympathetic fibers at a point where it leaves the main facial nerve gave rise to an ipsolateral rise in tension. Stimulation of the bilateral facial nerve fibers in the floor of the fourth ventrical gave rise to a bilateral increase in ocular tension. The rise in tension is thought to be caused by intraocular vasodilatation. (14 figures, 13 references)

I. E. Gaynon.

Heyman, Albert. **Discussion of ophthalmodynamometry as a diagnostic procedure.** Neurology **11**:104-106, April, 1961, pt. 2 (International Conf. on Vascular Disease of the Brain).

This article is mostly a restatement of data which also appear in the paper by J. F. Toole, appearing on pages 96-99 of the same issue of Neurology.

Thomas H. F. Chalkley.

Jones, R. F. **The syndrome of Marchesani.** Brit. J. Ophth. **45**:377-381, May, 1961.

The characteristics of the syndrome of Marchesani involve the body structure generally and the eye particularly. Brachycephaly, small short stature and short broad hands and feet with limitation of motion at the joints occur. In the eye there are spherophakia with microphakia, iridodonesis, visibility of the zonule, lenticular myopia and glaucoma. A brother and sister are briefly described who exhibited all the characteristic signs and symptoms and were children of consanguineous parents. In one child the progressive glaucoma did not respond to surface diathermy but was controlled with penetrating diathermy. In the younger child the glaucoma seemed to be controlled by pilocarpine. In both cases the myopia has continued to progress to a severe degree. (5 figures, 5 references) Morris Kaplan.

Kerdman, R. Y. **Bromine, barbiturates and vitamin B_1 effect on unconditioned vascular reflexes in glaucoma.** Vestnik Oftal. **4**:7-10, July-Aug., 1961.

A study of 25 glaucoma patients demonstrated that the administration of 0.5 percent or 1-percent bromine solution causes an activation of the unconditioned vascular reflexes. A single administration of luminal and vitamin B_1 had no noticeable effect on the state of the vascular reflexes. However, both bromine and vitamin B_1 have a favorable influence on the general condition of the patients in that the visual function is improved. These drugs are recommended as part of the pattern of glaucoma therapy. (1 table, 3 figures, 11 references) Benjamin Ziv.

Klutsevaya, E. E. **Iridentasis: antiglaucoma operation of wedging the iris into the suprachoroidal space.** Oftal. J. Ukraine **4**:237-242, 1961.

The new antiglaucoma operation, in which the iris is wedged into the suprachoroidal space, was successfully performed on 12 eyes of 12 patients with primary and secondary glaucoma. (8 figures) Benjamin Ziv.

Knox, D. L. **Glaucoma following syphilitic interstitial keratitis.** A.M.A. Arch. Ophth. **66**:44-51, July, 1961.

This entity presents some problems in diagnosis and management. The glaucoma usually appears many years after the acute keratitis and may resemble a chronic simple glaucoma or, less frequently, the onset may be acute. The author feels that intensive medical management is preferable to surgery. In one case histologic findings are described. (1 table, 4 figures, 10 references)

Edward U. Murphy.

Konstas, P. and Niesel, P. **Calibration of spring balance dynamometers.** Klin. Monatsbl. f. Augenh. **138**:714-717, 1961.

A simple device for calibration of spring balance ophthalmodynamometers is described. (4 figures, 1 table, 7 references) Gunter K. von Noorden.

Levene, R. Z. **Tonometry and tonography in a group health population.** A.M.A. Arch. Ophth. **66**:68-73, July, 1961.

A random sample of a large group health population was studied by means of Goldmann and Schiøtz tonometry and an attempt made to delineate normal findings. (2 figures, 6 tables, 15 references) Edward U. Murphy.

Perkins, E. S. and Jay, B. S. **Pigmentary glaucoma.** Tr. Ophth. Soc. U. Kingdom **80**:153-167, 1960.

Since 50 cases of pigmentary glaucoma have been reported, the authors feel that although it is rare such a condition does exist. From the published cases, the following facts emerge: the age of incidence is usually under 50 years, males outnumber females four to one, almost all patients have been myopic but not more than −4.00 diopters. Krukenberg spindles and other signs of pigment dispersion in the anterior chamber have been seen. Haloes were reported in many cases.

After studying 49 patients between the ages of 20 and 50 years of age, the authors concluded that there was an anomaly of the outflow system, myopia, and pigmentation. Pigmentary glaucoma is part of a larger syndrome consisting of a developmental defect in the outflow chambers, which is found most commonly in myopic males and the pigmentation is not the primary cause of the glaucoma but a contributing factor. (8 figures) Beulah Cushman.

Pilz, A. **Gonioscopic appearance and function test after Elliot's scleral trephination.** Klin. Monatsbl. f. Augenh. **138**: 826-833, 1961.

The efficiency of the fistula in eyes was determined after fistulizing glaucoma surgery. The functional test consisted of jugular vein compression and simultaneous registration of the arterial, venous, and intraocular pressures. These results were compared with the gonioscopic appearance of the chamber angle and the postoperative control of the pressure. Six case histories are reported. Sufficient drainage through the fistula, as determined by the function test, correlated well with adequate clinical control of the pressure. Discrepancies existed between the gonioscopic appearance of the fistula and its function. (11 figures, 12 references) Gunter K. von Noorden.

Řehák, S. and Vrána, M. **A contribution to the question of oculo-ocular pressure reactions in experimental animals.** Ophthalmologica **141**:253-261, March, 1961.

The present investigations are concerned with contralateral, intraocular pressure changes following various experimental ocular insults. The pressure was measured manometrically with a special device, since Schiøtz tonometry proved insufficiently exact. Four groups of experiments were carried out. In the first, by injecting saline solution into one eye of each of 20 rabbits, the pressure was raised gradually to 100 mm. Hg. This was accompanied by a 0.55 mm. Hg drop in the mercury column in the fellow eye, which was statistically significant! After five minutes the pressure had returned to normal. Secondly, the pressure in the eyes of 20 rabbits was decreased from 100 mm. Hg to 20 mm. Hg, after having been maintained at 100 mm. Hg for five minutes. This was accompanied by a statistically significant fall of 0.91 mm. Hg in the opposite eye. After five minutes the pressure was not significantly different from normal. Thirdly, the anterior chambers of six animals were simply punctured and the intraocular pressure

thereby abruptly reduced. In 30 seconds there was a 1.18 mm. Hg pressure drop in the companion eye, and at two minutes a 1.29 mm. Hg drop. Fourthly, 1 cc. of 15 percent NaCl solution was injected subconjunctivally in six animals. There was no significant change in the opposite eye in one minute, but a 2.88 mm. Hg rise in five minutes. At 10 minutes the pressure had returned to normal. The significance of these results is discussed at considerable length (leaving this reader not much wiser). (21 references)

Lawrence T. Post, Jr.

Rosa, D. **Clinical reports on glaucoma with detached retina.** Arch. di ottal. **65**: 25-44, Jan.-Feb., 1961.

The author reviewed all possible combinations of various types of glaucoma coexisting with various types of retinal detachment. Each of the 16 possibilities was documented by cases from the literature. The pathogenesis, when known, was described. Briefly, the types are as follows: detachment after absolute glaucoma, ideopathic detachment in glaucoma, detachment from medical or surgical hypotonia in glaucoma, glaucoma following detachment, traumatic detachment in glaucoma, traumatic glaucoma in detachment, detachment due to glaucoma surgery pulling the retina, cure of glaucoma after diathermy for detachment, detachment from miotic retinal pull, detachment and glaucoma due to inflammatory disease of the eye, detachment cured by hypertonia, glaucoma from adhesions of the iris and cornea in detachment, or from subluxation of the lens, detachment and hydrophthalmos in myopia, glaucoma and detachment in aphakia, and secondary detached retina with glaucoma. (52 references)

Paul W. Miles.

Tittarelli, R. **The effect of tartrate acid of 1-1-3'-4' diossiphenyl-2-metilam-minoctanolo (epinephrine bitartrate) on the ocular tension of glaucomatous patients.** Boll. d'ocul. **39**:873-890, 1960.

The author compared the effect on the intraocular pressure, of the instillation of 2-percent epinephrine bitartrate with other local and systemic anti-glaucoma medicaments, in 24 patients with chronic simple glaucoma and eight patients with hemorrhagic glaucoma. In all of these cases he found that the local instillation of 2-percent epinephrine bitartrate produced a significant lowering of the intraocular pressure, which was superior to that produced by the instillation of 10-percent phenylephrine chloridate. He also found that the epinephrine bitartrate 2-percent when combined with the topical administration of pilocarpine or the oral administration of diamox induced a further significant drop in the intraocular pressure. He also found that the reduction in the intraocular pressure induced by the combination of epinephrine bitartrate 2-percent and the administration of either pilocarpine (topical) or diamox (oral) was more effective than a combination of pilocarpine plus diamox alone. He feels that the instillation of epinephrine bitartrate is contraindicated in cases of closed-angle glaucoma. (12 tables, 17 references)

Joseph E. Alfano.

Toole, J. F. **Ophthalmodynamometry.** Neurology **11**:96-99, April, 1961, pt. 2 (International Conf. on Vascular Disease of the Brain).

The average deviation between the eyes in ophthalmodynamometry readings is about 5 percent systolic and 4 percent diastolic. In cases of occlusion of the internal carotid artery proximal to the origin of the ophthalmic artery, there should be a definite lowering of the retinal artery pressure as compared to the fellow eye. This test may also be used to determine the success of surgical restoration of the

carotid arteries. (4 figures, 16 references)
Thomas H. F. Chalkley.

Weinstein, Paul. **Optico-vegetative reflexes in the pathomechanism of glaucoma.** Tr. Ophth. Soc. U. Kingdom **80**: 225-228, 1960.

The author carried out tests to support the theory that the hypophysis does produce an intraocular-pressure-increasing principle owing to darkness. He was also able to prove that aniseikonia comes into being in a certain portion of the cases after the provocative effect of the dark room test. These cases usually occurred in hypertonic persons who also inclined to aniseikonia. It has also been observed that there was considerable increase in the adrenalin content of the blood as the result of darkness.

The effect of the cold pressor test in relation to light and darkness in glaucomatous and non-glaucomatous subjects has been named the photovasopressor reaction.

The author and his co-workers were able to observe that the effect of darkness in increasing the ocular tension does not occur merely mechanically in consequence of the dilatation of the pupil but also through an optico-vegetative reflex. They were able to confirm the fact that the pathomechanism of glaucoma involves, in addition to local mechanical reasons, neuro-vascular factors. The combination of both concepts shows the trend of future research work.

Sir Duke-Elder in discussing the paper drew attention to our relative ignorance of the anatomy of 20 percent of the optic nerve fibers which do not find their cell stations in the lateral geniculate body to be relayed to the occipital cortex. Some of these were pupillary afferent fibers, some constituted the photostatic opticotectal tract to the superior colliculus, but many went to the hypothalamos to find cell stations in the nuclei there. That an area of the hypothalamos acted as a controlling center of the intraocular pressure was now proved. Beulah Cushman.

Zamorani, G. **Microphthalmia and glaucoma.** Boll. d'ocul. **39**:746-758, Oct., 1960.

The author describes two cases of congenital microphthalmia with a high hyperopia and bilateral glaucoma. He felt that the glaucoma was due to an obstruction of the chamber angle by the disproportionately large and spherical lens. The glaucoma was progressive and failed to respond to miotic therapy. In one case the pressure was controlled with an iridencleisis and the other with a cyclodiathermy. Both surgical procedures were followed by a severe and prolonged uveitis. (4 figures, 2 references)
Joseph E. Alfano.

10
CRYSTALLINE LENS

Choyer, D. P. **The uses of all-acrylic anterior chamber implants.** Tr. Ophth. Soc. U. Kingdom **80**:201-218, 1960.

The author reports on the use of the transparent acrylic anterior chamber implants in 211 patients for correction of uniocular aphakia where contact lenses were unsuitable. Some cylindrical correction is usually necessary after introduction of an anterior chamber implant through a temporal incision.

Choyer lists the marked decline of serious complications in the second hundred cataract patients. The reduction in complications and the corresponding improvement in visual acuity can presumably be ascribed to the following factors: 1. the implants are made by machine tools, thus eliminating variations between implants, 2. improved sterilization of implants, 3. reduction in thickness of the haptic portion from 0.91 to 0.50 mm., 4. better selection of cases, and 5. improved surgical technique.

Attention is drawn to other possible

uses of wholly transparent implants in bilateral congenital cataracts, bilateral senile cataracts, uniocular high myopia, and in penetrating keratoplasty especially where the cornea is completely opaque and the history is scanty. There has been much less reaction to the anterior chamber implant than to the posterior chamber lens of Ridley. (6 tables, 6 figures)

Beulah Cushman.

Gramberg-Danielson, B. **On "secondary irradiation of the lens" during roentgenoscopy.** Klin. Monatsbl. f. Augenh. **138**: 711-713, 1961.

In a recent article (Klin. Monatsbl. f. Augenh. 136: 617, 1960) A. Jäger had suggested that the paradoxical subjective localization of X-rays striking the peripheral retina may be due to a scattering of rays while passing through the lens, and thus to a deviation from their original direction. The author postulates that for physical reasons the secondary irradiation from the lens cannot be effective enough to cause above threshold stimulation of the peripheral retina. (7 references)

Gunter K. von Noorden.

Haik, G. M., Kalil, H. H., Ferry, J. F. and Childers, M. D. **Subluxations and luxations of the lens: with a special note on the Barraquer operation and on Marfan's and Marchesani's syndromes.** Southern M. J. **54**:642-653, June, 1961.

Should one remove luxated or subluxated lenses only after iritis or glaucoma develops or remove them immediately if the patient is older than six years of age? The authors advocate the more aggressive approach, using the double-pronged needle of Barraquer-Calhoun. Luxations and subluxations of the lens are common in both Marfan's and Marchesani's syndrome. (21 figures, 13 references)

Thomas H. F. Chalkley.

Merdshanov, C. H., Bankov, P. and Yevtemov, K. **265 cataract extractions with a water pump erysiphake and Arruga forceps.** Oftal. J. Ukraine **4**:195-198, 1961.

The suction of the new erysiphake (Bankov, 1959) is created by a water pump installed either in the washroom or directly in the operating room. The power reaches 40 to 65 mm. of mercury in about five to eight seconds and is regulated by the water pump handle, which, in turn, is controlled by the surgeon's foot, thus leaving his hands free to manipulate the erysiphake.

The erysiphake consists of a puncture needle with a spoon-like attachment at one end, 3 to 5 mm. in diameter and 0.9 mm. thick. A ring is attached to the needle, 3 to 4 cm. from the spoon and perpendicular to it to give the erysiphake stability.

If a great deal of suction is applied, the anterior lens capsule is broken, and, in that case, an ideal extracapsular extraction occurs.

Comparative results of cataract extractions with the Arruga Forceps and the erysiphake are given: of 122 cataract extractions with the Arruga Forceps, 80.3 percent were intracapsular lens extractions, 19.7 percent extracapsular. In addition to two vitreous body prolapses, there were 10 percent various postoperative complications. Of 143 cataract extractions with the erysiphake, 87.4 percent were intracapsular lens extractions, 12.6 percent extracapsular, seven vitreous body prolapses, and 7.6 percent various postoperative complications.

The authors praise the extractions with the new erysiphake. (3 figures)

Benjamin Ziv.

Schrader, K. E. **Morphology and pathogenesis of experimental xylose cataracts.** Arch. f. Ophth. **163**:442-443, 1961.

Albino rats were examined periodically while on a diet containing from 15 to 35-percent d-xylose. Cataract formation be-

gan early in eyes having a patent hyaloid artery, but was less pronounced when insulin was given and in older animals. In the aqueous demonstrable xylose seems to be cataractogenic by blocking the carbohydrate metabolism of the lens. (13 figures, 62 references)

Harri H. Markiewitz.

Swan, H. T., Nutt, A. B., Jowett, G. H., Ferguson, W. J. Wellwood and Blackburn, E. K. **Monosemicarbazone of adrenochrome (adrenoxyl) and cataract surgery. Effect on capillary resistance and incidence of hyphaema.** Brit. J. Ophth. **45**: 415-422, June, 1961.

There was no apparent difference in the incidence of postoperative hyphema in a series of patients receiving oral adrenoxyl and those in the control group. (3 tables, 12 references)

Irwin E. Gaynon.

Tieri, O. **The concentration of cholesterol in the crystalline lens.** Arch. di ottal. **65**:57-63, Jan.-Feb., 1961.

The total cholesterol of beef lenses was determined repeatedly for 21 times. On the average, there was .228 milligrams per 100 milligrams of desiccated tissue with a range varying about 0.05 milligram. It was concluded that the cholesterol content of beef lenses is low and that it is not proportional to the lipid or to the water content. (10 references)

Paul W. Miles.

Waaler, Paul. **Age dispersion in patients with senile cataract during 1902-58.** Acta ophth. **39**:182-189, 1961.

On the basis of material drawn from the Eye Department in the Rikshospital in the time intervals of 1902 to 1909, 1922 to 1924 and 1957 to 1958 no age shift was found in the cataract patients admitted. A considerable uniformity and constancy in cataract dispersion prevailed throughout the period covered by the investigation. (4 tables, 1 reference)

John J. Stern.

Weinstock, M. and Stewart, H. C. **Occurrence in rodents of reversible drug-induced opacities of the lens.** Brit. J. Ophth. **45**:408-414, June, 1961.

The authors injected 31 morphine-like drugs into mice and produced an opacity of the anterior lens capsule. The cloudiness develops in a crescent shape, in the lower portion of the lens, and gradually spreads until the pupillary area is opaque. The effect begins within 15 to 20 minutes and becomes complete 20 minutes later. The eye clears within two to three hours. (3 figures, 1 table, 11 references)

Irwin E. Gaynon.

11
RETINA AND VITREOUS

Appelmans, M., Michiels, J., De Vloo, N., Jamotton, L. and Massa, J. M. **Lipemia retinalis in diabetics.** Arch. d'opht. **21**:5-13, Jan.-Feb., 1961.

The authors recall that the term "lipemia retinalis" was introduced by Heyl in 1880 to describe a rare pathologic ophthalmoscopic picture (9 cases in 11,000 diabetics, according to Joslin). They report a case in a 19-year-old girl, diabetic since the age of 11, who had suffered repeated episodes of hypoglycemic coma and showed, at the time of the lipemia retinalis, an abnormal lipidogram. Blood studies revealed a lipid level of 4,300 mg. percent and a cholesterol level of 1400 mg. percent. Visual function was unaffected and there was no trace of lipid infiltration of the cornea nor of lipid in the aqueous. With insulin treatment and regulation of diet, the ophthalmoscopic picture returned to normal in ten days. (2 figures, 39 references)

P. Thygeson.

Ashton, N., Pears, M. A. and Pickering, G. W. **Neuroretinopathy following haem-**

orrhage with a discussion on the nature of cytoid bodies. Brit. J. Ophth. **45**:385-394, June, 1961.

Hemorrhage may provoke 1. sudden blindness with swelling of the disc or optic atrophy, and 2. neuroretinopathy resembling that of malignant hypertension. In the patient who is the subject of this case report, the exudates appeared to attain their maximum size within 12 hours. The exudates were limited to the posterior pole of the eye. Sections showed massive edema with many cytoid bodies in the stratum opticum of the retina. A close relationship to the arteriole was noted. Fatty degeneration was present. The cotton-wool exudates are confined to the nerve-fiber layer at the posterior pole, are multiple and situated close to the main vessels, and are probably secondary to the focal ischemia. (8 figures, 39 references) I. E. Gaynon.

Clara, Max. **Studies on the basal membrane of retinal capillaries.** Arch. f. Ophth. **163**:448-463, 1961.

Eyes of man, dogs, guinea pigs and pigs were fixed in various solutions and histologically stained by a multitude of methods. The basal membrane is situated between the capillary endothelium and retinal tissue. Submicroscopically, it is a complex structure built of protein, mucopoylsaccharides, and lipids, but without argyrophile fibers. (4 figures, 96 references) Harri H. Markiewitz.

Connor, P. J., Jr., Juergens, J. L., Perry, H. O., Hollenhorst, R. W. and Edwards, J. E. **Pseudoxanthoma elasticum and angioid streaks: a review of 106 cases.** Am. J. Med. **30**:537-543, April, 1961.

Pseudoxanthoma elasticum is inherited either as a recessive or an irregularly dominant trait. Frequently associated angioid streaks in the retina result in the designation "Groenblad-Strandberg syndrome." Angioid streaks are cracks in Bruch's membrane caused by degeneration of the elastic material composing this structure. In a majority of cases maculas become involved and bilateral macular degeneration results. (4 figures, 1 table, 18 references)

Thomas H. F. Chalkley.

Cristiansson, J. **The collagen content of the vitreous body in alloxan diabetic rabbits.** Acta ophth. **39**:141-147, 1961.

There was a significant reduction in the total amount of hydroxyproline in the collagen network of the vitreous body of alloxan diabetic rabbits as compared to normal animals. The hyaluronic acid content in the diabetic rabbits was considerably increased and therefore the ratio of hyaluronic acid to collagen is markedly changed. (1 figure, 9 references)

John J. Stern.

Czukrász, I. and Schlammadinger, J. **The etiopathogenesis of the Groenblad-Strandberg syndrome (pseudoxanthoma elasticum).** Orvosi Hetilap **102**:1177-1180, 1961.

The case histories of three patients with the Groenblad-Strandberg syndrome are described. The authors point out the variability of the disease pattern and emphasize the importance of an increased cooperation between the various branches of medicine, which, as they hope, will increase the number of recognized cases. The authors state that the present therapeutic methods produce rather poor results. Gyula Lugossy.

Ericson, L. A. Gothenburg and Fluur, E. **Electro-oculographic studies during treatment for retinal detachment.** Acta ophth. **39**:222-230, 1961.

Twenty-one patients who had been operated on for retinal detachment and were being kept in bed with a binocular bandage were examined by means of an electro-oculogram. In several of the younger

patients a considerable oculomotor activity could be shown. In elderly patients the electro-oculograms took a much more level course. In view of these lively eye movements in blind-folded patients with retinal detachment, it is suggested to immobilize the eye possibly with episcleral sutures. Stenopaeic spectacles provided adequate fixation and moderate eye movements; the eyeball was able to deviate only about 10 degrees in all directions. (4 figures, 6 references) John J. Stern.

Filatova, Z. A. **The prognostic meaning of the height of intraocular pressure in detached retinas.** Oftal. J. Ukraine **3**:174-178, 1961.

In a study of 175 cases of detached retinas in 150 patients, 68 percent were found to have normal intraocular pressure. This is contrary to the opinion that ablatio retinae is always accompanied by hypotension.

Changes in intraocular pressure occur most often either in the first three months or after one year of this disease. The disturbance in intraocular pressure is more frequent in cases of total ablatio retinae. A drop in intraocular pressure indicates a poor prognosis. (5 tables, 4 references) Benjamin Ziv.

Fischer, F. **Unusual remissions in retinitis diabetica proliferans.** Arch. f. Ophth. **163**:397-402, 1961.

The data on four patients with advanced retinopathy in whom visual acuity remained stationary for four years are briefly recorded. (10 references) Harri H. Markiewitz.

Goddé-Jolly, D. **Photocoagulation in the course of Eales' disease.** Arch. d'opht. **21**:14-19, Jan.-Feb., 1961.

The author states that photocoagulation has been used with some success in Eales' disease. He reviews in detail the indications and technique of operation and discusses the protean nature of the Eales' syndrome and the character of the vessel changes for which photocoagulation is advocated. He then describes 72 cases with periphlebitis, 55 of which had recurrent hemorrhages. Of these 55 cases, eight were photocoagulated. The results appear to have been good but sufficient time has not elapsed for final judgment. The author concludes that 15-20 percent of periphlebitis appears to be suitable for coagulation and at various intervals after operation. A bibliography of 20 references is appended. (3 figures, 20 references) P. Thygeson.

Godde-Jolly, D. and Bonnin, P. **Retinal lipemia.** Ann. d'ocul. **194**:674-693, Aug., 1961.

The authors report the case of a 46-year-old man, a known diabetic, who presented himself with a complaint of diminished vision. He was also a heavy imbiber of alcohol and was a rather heavy smoker. Examination of the fundi showed a typical picture of lipemia retinalis. The lipid content of the blood was 92 grams per liter. In addition it was found that the patient was in acidosis. Treatment of the acidosis quickly resulted in a reversal of the retinal lipemia. Although ethyl alcohol has been reported to be a cause of retinal lipemia, the authors feel that this case was entirely on the basis of diabetic acidosis. (3 figures, 2 tables, 107 references) David Shoch.

Imre, Gy. and Tóth, M. **Periphlebitis retinae.** Szemészet **98**:92-95, 1961.

Relying upon the evidence obtained in 54 cases of periphlebitis, the authors claim that in view of the poor results produced by antituberculosis therapy, the tuberculous origin of periphlebitis retinae is questionable and certainly not proved. Endocrine or allergic factors, even viral infection, may play a role in the etiology of the disease. Gyula Lugossy.

Jonkers, G. H. **Equatorial encircling of the globe for treatment of retinal detachment.** Klin. Monatsbl. f. Augenh. **138**:790-797, 1961.

In 1957 Arruga advised encircling of the globe with a nylon, silk, or supramid thread. This method is technically considerably less difficult than the Schepens procedure. The author reports his good experiences with the Arruga technique which was applied in 13 patients with detachment. (3 figures, 2 tables, 5 references) Gunter K. von Noorden.

Meroshnekova, L. M. **Local dark adaptation in detached retinas.** Oftal. J. Ukraine **3**:171-174, 1961.

A study of local dark adaptation in a 3° field was made on 22 patients with detached retinas, 15 of whom were used as postoperative controls. Myopia was the most common origin of the detached retinas.

The following conclusions were given: local dark adaptation in detached retinas is absent or almost absent in the pathological field as well as in the intact visual field. (Sometimes, in the intact visual field the abnormal area manifests itself by a slow adaptation.)

Changes in dark adaptation do not have any proportional relation to the pathological areas of the visual field. Improvement in the ability to dark adapt after surgery is indicative of a favorable prognosis. (4 tables, 5 references)

Benjamin Ziv.

Pedler, Christopher. **The inner limiting membrane of the retina.** Brit. J. Ophth. **45**:423-438, June, 1961.

It seems probable that the granular layer overlying and infiltrating the retinal mosaic is formed partially by the hyaluronic acid type of mucopolysaccharides. The inner limiting membrane has different staining properties than the radial fibers. The radial fibers are firmly attached to the limiting membrane. The outer surface of the spinal cord is embryologically equivalent to the inner aspect of the retina. Both arise from the same surface of the primitive central nervous system. (12 figures, 24 references)

Irwin E. Gaynon.

Rosengren, B. **Scleral buckling by means of a silver ball in detachment surgery.** Tr. Ophth. Soc. U. Kingdom **80**: 219-224, 1960.

The author discusses the use, at the clinic in Gotenborg, Sweden, of a silver ball or cylinder 4 mm. in diameter and mounted on an arm projecting from the periphery. The silver ring is attached to the sclera anteriorly and the ball is pressed against the sclera accurately in position with the scleral bulge contacting the retinal tear. Cauterization can then be done with the aid of diathermy or with light coagulation.

The scleral depressor causes surprisingly little irritation, which seems to be alleviated by instillation of cortisone drops. The ball becomes coated with capsular tissue and should not be applied longer than three or four weeks.

The silver ball method is best suited for single tears and those in the posterior portion of the retina. It is not suitable for eyes with several ruptures but has the advantage of getting rid of subretinal fluid without actual drainage. (1 table, 4 figures) Beulah Cushman.

Ruedemann, A. D. and Noell, W. K. **The electroretinogram in central retinal degeneration.** Tr. Am. Acad. Ophth. **65**: 576-594, July-Aug., 1961.

Fifty-five normal subjects were studied and compared with 50 who had central retinal degeneration. The latter group was divided into five subgroups: juvenile and adult familial central pigmentary de-

generation; Kuhnt-Junius disease, senile macular degeneration, macular chorioretinitis, and retinitis pigmentosa. In addition to a routine eye examination including visual fields, electroretinograms were done under photopic and scotopic conditions, using various colored stimuli and using flicker.

Five cases are presented in detail. An overall reduction in electroretinographic amplitudes and responsiveness was found. Specific changes also were noted, but no definite conclusions are drawn from them. The value of electroretinography appears to lie in differentiating central and peripheral disease, and retinal versus pathway disease; in assessing covert bilaterality; in determing preclinical familial conditions; in objectively assaying the results of therapy; and in elucidating the nature of the ailment. (34 figures, 14 references) Harry Horwich.

Vécsei, A. **Alteration of retinal vessels in diabetes mellitus.** Szemészet **98**:87-91, 1961.

The author examined the characteristic retinal aneurysms seen in 30 patients with longlasting diabetes who had died from various causes. The aneurysms may grow to such an extent as to penetrate all layers of the retina and to displace its tissues. The vessel wall thickens and displays signs of degeneration, and its permeability undergoes alteration. Because of the change of permeability blood and exudate leak into the vicinity and may reach even the macular region through the loose texture of the retina, giving rise to eventual vitreous hemorrhages. These complications are accompanied by severe visual impairment and may lead even to loss of sight. Gyula Lugossy.

12

OPTIC NERVE AND CHIASM

Chun, R. M. W., Smith, N. J., and Forster, F. M. **Papilledema in Sydenham's chorea.** Am. J. Dis. Child. **101**:641-644, May, 1961.

This is the second well-documented report of papilledema in a patient with Sydenham's chorea. The papilledema was bilateral and resolved in about two weeks, with no residual defects of field or vision. (29 references) Thomas H. F. Chalkley.

Collier, M. **Some rare pathologic associations with hyaline excrescences on the disc.** Ann. d'ocul. **194**:699-732, Aug., 1961.

The author describes 16 cases of drusen of the optic nervehead. In the study of these patients he found that other anomalies were frequently present. In two patients there was an associated corneal dystrophy, in another congenital lenticular opacities, and in others some unusual malformations of the retinal vessels. The non-ocular anomalies included diabetes, telangiectases, and nevi. A final group consists of a father and daughter, both of whom showed evidence of Friedreich's ataxia. (27 figures, 23 references) David Shoch.

Kittel, V., Goder, G. and Kittel, E. **Clinical features and histology of meningiomas of the optic nerve.** Klin. Monatsbl. f. Augenh. **138**:664-672, 1961.

Clinical course and histological studies of two cases are reported. One patient was 39, the other 40 years old when the first symptom (exophthalmos) occurred. It is surmised that meningiomas of the optic nerve originate from cells of the neural crest, and should accordingly be termed mesectodermal tumors. (10 figures, 15 references) Gunter K. von Noorden.

13

NEURO-OPHTHALMOLOGY

Bozzoni, F. **A case of post-traumatic oculo-palpebral synkinesis due to abnor-**

mal regeneration of the third cranial nerve. Boll. d'ocul. **39**:919-927, 1960.

The author presents a case of misdirection of regenerating left third nerve fibers after a traumatic fracture of the left parietal bone. The patient demonstrated a left ptosis with a paresis of the left medial and superior rectus muscles. Attempted adduction of the left globe produced a widening of the left palpebral aperture. The author proposed to perform a 10 mm. resection of the left medial rectus muscle, followed by a tenotomy of the left superior palpebral muscle and the subsequent attachment of the latter muscle to the frontales muscle. Following an 11 mm. resection of the left medial rectus muscle the eyes were cosmetically aligned, but an intervening illness prevented the surgery of the levator muscle. (2 figures, 22 references) Joseph E. Alfano.

Dyereng, S. A. and Shachayev, O. V. **Stable accommodation spasm in diseases of the central nervous system.** Vestnik Oftal. **3**:51, May-June, 1961.

The authors cite three cases of stable spasm of accommodation occurring after a brain concussion or encephalitis. Corrective methods did not improve the resulting decrease in visual function of which the patients complained. The accommodative spasm was accompanied by a convergence spasm. Atropine was found to remove the accommodation spasm only temporarily. Benjamin Ziv.

Guth, L. and Bailey, C. J. **Pupillary function after alteration of the preganglionic sympathetic innervation.** Exper. Neurol. **3**:325-332, April, 1961.

The superior cervical sympathetic ganglion was partially denervated in 21 cats, resulting in complete interruption of the preganglionic fibers to the pupil. The pupil immediately became miotic but gradually returned to normal in the course of the next 36 weeks. The restoration of tonus was due to the development of collateral sprouts from residual nonpupillary fibers within the ganglion. (2 tables, 1 figure, 14 references)

Thomas H. F. Chalkley.

Olivarius, B. de F. and Jensen, L. **Retrobulbar neuritis and optic atrophy in pernicious anemia.** Acta ophth. **39**:190-197, 1961.

The literature is reviewed and two cases are presented in which retrobulbar neuritis occurred together with pernicious anemia. It is stressed that the occurrence is very rare, in fact in the two cases under review the diagnosis is doubtful. Nevertheless it is most important to think of pernicious anemia as a causative factor in otherwise unexplained retrobulbar neuritis. (28 references)

John J. Stern.

Panfelova, G. V. **Skull bone lesion in neurofibromatosis (Recklinghausen).** Oftal. J. Ukraine **4**:217-221, 1961.

Although neurofibromatosis is difficult to diagnose from skull bone lesions only, the lesions together with other clinical data help to arrive at the correct diagnosis. Enlargement of the orbit, thinning of its walls, changes in the anterior and middle parts of the skull are the usual seat of the X-ray findings in this disease. The author presents six cases. (4 figures, 9 references) Benjamin Ziv.

Riklan, M. and Diller, L. **Visual motor performance before and after chemosurgery of the basal ganglia in Parkinsonism.** J. Nerv. & Ment. Dis. **132**:307-314, April, 1961.

The Bender Visual Motor (Gestalt) test was administered to 54 patients with Parkinson's disease before and after chemosurgery of the basal ganglia. Those having surgery on the right hemisphere became worse in their performance immediately postoperatively and then grad-

ually improved to their preoperative levels. Those having surgery of the left hemisphere had no change immediately postoperatively and an improvement in long-range performance. It seems that there are different functions for the hemispheres, the right being more significant, at least as far as this test is concerned. (3 tables, 25 references)

Thomas H. F. Chalkley.

Segelov, J. N. and Davis, R. **Towards earlier diagnosis of brain tumours.** Med. J. Aust. 11:1-6, 1961.

A series of 700 cases of intracranial tumor is reviewed. Symptoms had often been present for a long time before the patients had a neurologic investigation. Although found frequently, the triad of headache, vomiting and papilledema occurs relatively late. Epilepsy beginning in adult life requires full investigation before anti-convulsants are ordered. The onset of unilateral deafness may mean the presence of an acoustic neuroma.

Ronald Lowe.

14
EYEBALL, ORBIT, SINUSES

Tengroth, Björn. **The effects of D-thyroxin in experimentally TSH-induced exophthalmos in guinea pigs.** Tr. Ophth. Soc. U. Kingdom 80:131-136, 1960.

The author assumes that loose connective tissue in general is influenced both by the pituitary hormone thyrotropin or the exophthalmotropic factor and by the thyroid hormone thyroxin. Thyrotropin causes an increase in water-binding substances and thyroxin has an antagonistic effect causing a decrease in volume. It is therefore probable that endocrine exophthalmos can be caused by this thyrotropic connective tissue reaction in the orbit especially in the eye muscles. From this point of view one can expect the endocrine exophthalmos to be diminished by giving thyroid hormone.

Thyroidectomized guinea pigs treated with daily injections of 3 USP units of Organon TSH develop a measurable exophthalmos after 24 hours. Fifty animals were studied and it was found that the exophthalmos developed according to the dosage. Physiologically d-thyroxin and l-thyroxin are found; the d-thyroxin is supposed to have less than 1/10 of the metabolic effect of l-thyroxin. The animals injected with 0.4 mg. of d-thyroxin per day did not develop any significant exophthalmos; l-thyroxin produced the same astigmatic effect as the d-thyroxin without having the metabolic thyrotoxic effect.

Case reports illustrate the discussion.

Beulah Cushman.

Tengroth, B. **Endocrine exophthalmos. Effects of thyrotropin preparations and the thyroxin isomers. Quantitative evaluations in guinea pigs.** Acta ophth. Supplement 65, 1961.

After reviewing earlier investigations of 1. the hormonal origin of endocrine exophthalmos, 2. anatomic changes associated with it and 3. the influence on it of thyroid hormone and thyroxin, the author reports his own investigations. Adult male albino guinea pigs, thyroidectomized and normal, were used to study the development of exophthalmos following treatment with the thyroid preparation TSH Organon with Sodium d- and sodium l-thyroxin. Changes in eye position were recorded roentgenographically. Sixty percent of the difference between measurements was accounted for by the ability of the animals to change their eye position; the error of the method amounted to 0.1 to 0.2 mm. Drying of the tissues examined was carried out in a vacuum of 10^{-3} mm. mercury at room temperature.

Treatment with TSH was started immediately after, and seven days after thyroidectomy and continued for 13 days.

Exophthalmos resulted and was greater in the animals in which the hormone was withheld for seven days. In normal control animals TSH did not produce exophthalmos. Tissue examinations showed that thyrotropin preparations containing an exophthalmos producing factor cause an increase of fluid in the eye muscle and in Harder's gland; it can be recorded before measurable exophthalmos appears; the same fluid increase can be found in skeletal muscles. D-thyroxin inhibits the development of the exophthalmos produced by thyrotropin preparations in thyroidectomized animals, and it also inhibits the fluid increase in the extraocular muscles and Harder's gland; no difference was found in this respect between d- and l-thyroxin. (16 figures, 156 references)

John J. Stern.

15

EYELIDS, LACRIMAL APPARATUS

Baken, L. M. **Hammer-free instruments for dacryocystorhinostomy.** Vestnik Oftal. **3**:68-69, May-June, 1961.

The author introduced a trephine cutter for bone drilling, thereby eliminating hammering in dacryocystorhinostomy. (1 figure, 13 references) Benjamin Ziv.

Boles Carenini, B. and Lodi, M. **The measurement of the contraction power of the orbicularis muscle in normal subjects.** Boll. d'ocul. **39**:859-872, 1960.

The force of contraction of the orbicularis oculi muscle in normal subjects was determined, using a speculum with a graduated increasing-power spring. The relationship between age, sex and the right and left side was determined. The normal force of contraction appeared to be about 76.8 grams. The force of contraction is greater in the male than the female, and increases to the age of 40 years, after which it declines. There was no statistical difference between the right and left sides. The authors feel that this instrument may be of some value in determining the effect of anesthetic agents on the force of contraction of the orbicularis oculi muscle. (5 figures, 6 tables, 3 references) Joseph E. Alfano.

Ellison, J. **Hydrops of lid.** Tr. Ophth. Soc. U. Kingdom **80**:229-230, 1960.

The author applies this term to intermittent swelling of the lids, a condition which causes discomfort and pain and also interferes with vision. Chronic nephritis and myxedema were ruled out. The author drained the right lower lid and found the cell contents the same as in circulating blood. He evaluated the fluid and left a nylon drain in the dependent part. Later he removed the excess tissue and the patient was free from trouble and remained so. (1 figure)

Beulah Cushman.

Isaksson, Ivar. **A study in congenital blepharoptosis.** Tr. Ophth. Soc. U. Kingdom **80**:23-238, 1960.

Congenital drooping of the upper eyelid is a descriptive term for a dysfunction of the lifting mechanism of the upper eyelid. It is usually apparent shortly after birth and can be uni- or bilateral, partial or complete. It occurs in both sexes and is more common in the male. The degree of ptosis may remain the same or unchanged for many years, or may grow considerably worse. This abnormality is definitely in the levator palpebrae superioris muscle. In 30 cases classified as genuine congenital blepharoptosis, the author found pathologic changes in the muscle. Tissue for histologic study was obtained from patients whose deformity has been corrected by Blaskovicz's technique.

Slight to extensive degenerative changes occurred in the muscle fibers and sometimes atrophy with groups of sar-

colemma nuclei was noted. Within some fields the muscle fibers were wholly or partly missing, and there was a great deal of immature connective tissue and large numbers of plasma cells and lymphocytes. In some places muscle fibers had been entirely replaced by hyalinized sclerotic tissue. The lesion appears to be histologically progressive and fibrosis represents the final stage. The pictures correspond to what the pathologists call primary muscular dystrophy. The electromyographic studies of the levator correspond to the aforementioned microscopic changes. The levator is capable of lifting the upper lid but not of holding the open position. Patients with ptosis may also have a functional weakness in their superior rectus muscle, and occasionally also a weakness of the inferior oblique muscle. Changes shown microscopically cannot be distinguished from those in progressive muscular dystrophy in the skeletal musculature, therefore the author feels that blepharoptosis is a topographically definable form of progressive muscular dystrophy. (5 figures)

Beulah Cushman.

Leibiger, W. **A rare secretional anomaly of the Meibomian glands.** Klin. Monatsbl. f. Augenh. **138**:876-880, 1961.

The anomaly was observed in a 56-year-old man and consisted of long, greenish filamentous secretory products of the Meibomian glands. The glands had to be expressed frequently during the past six years. Occasionally, cystic swellings were observed in the lids. (2 figures, 10 references) Gunter K. von Noorden.

Peelman, N. E. and Vegrizer, G. Z. **Tumor-like palpebral formation spreading into the orbit.** Vestnik Oftal. **4**:43-45, July-Aug. 1961.

A tumor-like palpebral proliferation developed soon after a mild conjunctivitis. Trachoma was absent. According to clinical and morphologic studies, the disease which is rare and difficult to diagnose is characterized by amyloidosis, subconjunctival granuloma, inflammatory tumor-like swelling, tarso-conjunctival degeneration, and a tumor-like swelling of the conjunctiva spreading from the lids to the orbit. (12 references) Benjamin Ziv.

Somerset, E. J. **"Spider lick" an epidemic ophthalmodermatozoosis due to beetles of the genus paederus.** Brit. J. Ophth. **45**:395-407, June, 1961.

"Spider lick" is a lesion of the skin produced by contact with beetles of the genus paederus. The hindmost part of the beetle contains a vesicating substance. The lesion consists of weals with a central yellowish line of coagulated superficial cells. The lesion appears 24 hours after contact and lasts several days; it responds well to antihistaminics. It is common in India. (5 figures, 3 tables, 60 references) Irwin E. Gaynon.

Svyadosh, B. E. **The treatment of palpebral skin cancer.** Vestnik Oftal. **3**:3-7, May-June, 1961.

Because X-ray therapy has been so successful in palpebral skin cancer, it has eliminated surgery. Regardless of the location of the tumor, in addition to restoring the organ's ability to function, X-ray therapy has proved to be of good therapeutic and cosmetic value.

Of 514 cases in which close-focus X-ray therapy (X-ray apparatus made in U.S. S.R.) was used, 94 percent of the patients recovered after one series of irradiation and only 6 percent required additional treatment before complete recovery. The results of close-focus X-ray therapy are independent of the histologic architecture of the palpebral skin cancer. Neither the blood nor organisms showed any side-effects. (1 table, 15 figures, 10 references)

Benjamin Ziv.

Wilczek, M. **Reconstructive surgery of the lids.** Klin. Monatsbl. f. Augenh. **138**: 805-810, 1961.

A method is described to cover defects of upper or lower lid by sliding skin grafts. Four cases are reported and the results illustrated. (15 figures, 6 references) Gunter K. von Noorden.

16
TUMORS

Goetze. **Differential diagnosis of rare tumors in the anterior segment of the eye.** Klin. Monatsbl. f. Augenh. **138**:657-663, 1961.

Cases of hemangioma and elastoidosis of the lids, benign lymphadenosis and malignant degeneration of a formerly benign pigmented nevus of the conjunctiva, and ectopic lacrimal glands are reported and illustrated. (12 figures, 9 references) Gunter K. von Noorden.

Machado, N. R. **Malignant melanoma secondary in the orbit.** Arq. brasil. oftal. **23**:207-220, 1960.

This is an interesting case report of a 32-year-old white man whose inflamed, painful eye which had been blind for two years as the result of trauma was eviscerated. Shortly after the evisceration, a rapidly growing tumor appeared in the orbit, which was exenterated. The patient had a progressive deterioration of his general condition and died three months later from cachexia and liver metastases.

Pathologic examination of the specimen indicated the presence of malignant melanoma with a probable origin in the uveal tract. There was invasion of the optic nerve and the extraocular muscles. (10 figures, 8 references.

James W. Brennan.

Thiel, R., Otto, J. and Toppel, L. **Statistical studies of intraocular malignant melanomas and retinoblastomas.** Klin. Monatsbl. f. Augenh. **138**:682-704, 1961.

Follow-up examinations on 166 patients with malignant melanoma and 32 patients with retinoblastoma, both diagnoses histologically confirmed, were conducted since 1935 at the University Eye Clinic in Frankfurt. The data on frequency, age and sex distribution, localization, and survival rate were analyzed statistically.

The number of patients with malignant melanoma has increased in recent years. The highest incidence in women occurred between 40 and 50 years of age; and between 50 and 60 years in men. One hundred forty six (88 percent) of the patients had choroidal lesions and 12 (7 percent) had iris or ciliary body lesions. In 58 patients who were controlled over periods up to 15 years, the survival rate could be determined. One half of the patients had died three and three-fourths years after enucleation. The majority died from liver metastases.

Retinoblastoma occurred most frequently in children in their first or second year of life. No significant difference existed in the sex distribution. Twelve out of 33 subjects had bilateral lesions. Of 21 patients with monocular retinoblastoma nine lived longer than five years after enucleation; three are still alive after three years.

Enucleation and therapeutic procedures other than removal of the globe, such as light coagulation, diathermy coagulation, irradiation with X-rays and cobalt, and chemotherapy are discussed and evaluated on the basis of the authors' own experience. (4 figures, 1 table, 52 references) Gunter K. von Noorden.

17
INJURIES

Blatt, N. and Athanasiu, M. **Technique and plan for the exact localization and extraction of a large foreign body situated**

on the sclera and optic nerve. Arch. d'opht. **21**:20-32, Jan.-Feb., 1961.

The authors believe that the chief difficulties that arise in extracting foreign bodies from the orbit are due to faulty localization. They review in detail the localizing methods available and stress the value of stereoradiographic, tomographic, and radiokinetic techniques. The foreign bodies most difficult to localize are those lying directly on the globe or optic nerve, or in or between the recti muscles. The authors report the case of a patient with a retrobulbar metallic foreign body received four years previously when an unsuccessful attempt to extract it had been made. Suddenly pain and diminished vision, with concentric field contraction, developed and required immediate surgery. Radiographic study revealed a large foreign body in the orbit on the sclera next to the nerve; the body moved simultaneously with the globe but with sufficient variation to indicate clearly that it was not attached to the globe. Extraction of the body (8 × 3½ mm. in size) was accomplished by superior-nasal orbitotomy without damage to major orbital tissues. After surgery the vision improved from hand movements to 5/30 and the field became significantly enlarged. The authors advocate early localization and extraction of all metallic orbital foreign bodies. (6 figures) P. Thygeson.

Dahlberg-Parrow, Ragna, **Intraocular glass foreign body extracted after 14 years.** Acta ophth. **39**:168-170, 1961.

A piece of glass which had penetrated into the eye suddenly migrated into the anterior chamber after 14 years. The injury had caused a cataract which had been removed and the foreign body managed to migrate through a very small opening in the lens capsule residues. It was removed with the help of Flieringa's ring. (7 references) John J. Stern.

Darabos, Gy. and Gombos, K. **The effect of ultrasound on the blind spot.** Szemészet **98**:101-106, 1961.

The authors studied the reaction of the blind spot to irradiation with ultrasound, Sollux lamp and short wave, respectively. In almost all cases enlargement was found. One hour after completing the irradiation it was observed that the blind spot had been reduced as compared to its pre-treatment extent, possibly owing to the increased metabolism.

Gyula Lugossy.

Hudomel, J. **Foreign bodies at the chamber angle.** Szemészet **98**:82-86, 1961.

The author sums up his experiences on injuries in the vicinity of the chamber angle; in nine patients at the Eye Clinic, Budapest University Medical School. He draws attention to the importance of exact anamnesis and emphasizes the necessity for clarifying the circumstances under which the injury occurred. If X-ray localization by Sweet's or any other technique fails, the author regards a Vogt's bone shadowless radiography as essential. He points out the limits of error of the radiologic methods used in the surgery of these injuries. In case of a negative radiological result, he holds it indispensable to carry out gonioscopy, which is the only procedure for making X-ray-negative foreign bodies of the angle visible. In order to remove a free and magnetizable foreign body a direct incision just above it should be made, whereas for approaching an encapsuled or fixed, non-magnetizable one a modification of Haab's operation is recommended. Gyula Lugossy.

Zeppa, R. **A case of palpebral ptosis and mydriasis from viper bite.** Arch. di ottal. **65**:21-24, Jan.-Feb., 1961.

A patient, aged 32 years, was bitten on the foot by a viper. For 48 hours he had ptosis and mydriasis without loss of vi-

sion or visual field. The pathogenesis and treatment are discussed. (8 references)
Paul W. Miles.

18
SYSTEMIC DISEASE AND PARASITES

Agnello, F. **Clinical approach to eclamptic amaurosis.** Boll. d'ocul. 39:657-663, 1960.

The author describes the fundus pictures of two young patients with eclampsia of pregnancy. The fundus changes consisted of arteriolar spasm with retinal ischemia. After delivery the visual acuity and fundus picture returned to normal. (13 references) Joseph E. Alfano.

Bourke, G. M. and Yeates, F. M. **Blindness due to household pets.** Med. J. Aust. 11:12-14, 1961.

The life cycle of Toxocara canis and the mode of infestation of man are described in detail. General and ophthalmic lesions are described. Two cases are presented, one in a patient with generalized lesions and one with a blind left eye. Preventive measures are stressed and are as follows: (1) Pups should be given effective anthelminthic treatment at least six times during twelve months; (2) Children should not be allowed to touch a bitch nursing puppies and her feces should be effectively destroyed; (3) The fur and feces of puppies are dangerous for children.
Ronald Lowe.

Collier, M. **Progressive myopathy of the Landouzy-Dejerine type and ocular melanosis.** Ann. d'ocul. 194:607-613, July, 1961.

43-year-old woman presented a picture of facio-scapulo-humeral atrophy (Landouzy-Dejerine) associated with a limbal melanosis and a melanotic plaque of the lid. Both the patient and a sister showed slowed pupillary reflexes and in addition the sister had acute episodes of vertical diplopia and a pigmented lesion of the cheek. (2 figures, 29 references)
David Shoch.

Gros, C., Cazaban, R. and Yassis, A. **Ophthalmologic aspect of the craniostenoses.** Ann. d'ocul. 194:615-626, July, 1961.

The craniostenoses have in common a premature synostosis of the bony sutures of the calvarium. Different forms such as scaphocephaly, brachycephaly, and oxycephaly, evolve on the basis of the sutures which are involved.

The cardinal eye signs of this disease are exophthalmos, strabismus, hypertelorism, poorly reactive pupils, and later, optic atrophy. The only treatment of value is a decompression of the skull and this should be done as soon as the diagnosis is established, and if possible before the age of four years. This should precede any ophthalmologic intervention by at least one year. 29 references) David Shoch.

Smith, V. H. **Carotid insufficiency.** Tr. Ophth. Soc. U. Kingdom 80:253-262, 1960.

These studies with animal experiments on the rabbit concern the pressure in the ophthalmic artery during carotid occlusion. A needle connected to a pressure apparatus was introduced into the anterior chamber and the intraocular pressure was raised above that in the ophthalmic artery. A vital dye (pontamine sky blue) was then injected intravenously; if the intraocular pressure was reduced below that in the ophthalmic artery the retina stained blue, if it remained above the pressure in the ophthalmic artery no dye entered the eyes and the retina retained its natural color.

Experimentally differences of more than 15 percent in the systolic and 10 percent in the diastolic pressures of the two sides are suggestive of carotid occlusion. The author believes that 20 percent is the smallest difference between the systolic readings that should be accepted as indicating carotid occlusion. Monocular symptoms associated with carotid occlusion may be due to a simple fall of pressure due to carotid block. Ophthalmody-

namometry provides a safe and reliable method of diagnosis in carotid occlusion.

Beulah Cushman.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Antyalava, D. N. **The first scientific ophthalmological meeting of the Georgian Republic of the U.S.S.R. held in Tbelece, Feb. 23-26, 1961.** Vestnik Oftal. 4:93-95, July-Aug., 1961.

Among diverse papers presented at the meeting was one by V. E. Tsentsadze who recommended a study of the state of local light adaptation in the peripapillar retinal zone. A positive water drinking test promotes a lowering of the light sensitivity level. Tsentsadze believes that this test could help in early diagnosis of glaucoma.

A summary of a paper by T. A. Alexedze showed that smoking disturbs the ocular tension; i.e., it increases the pressure for a short span of time.

Benjamin Ziv.

Cafragna, M., Latte, B., Rattazzi, M. and Siniscalco, M. **An isolate of congenital hemeralopia in Sardinia. Data on families and population.** Boll. d'ocul. 39:891-905, 1960.

The authors discuss the incidence of night blindness in a small village in Sardinia. The size of the village over the past 50 years has been almost 2,000 people. The average number of children per family was 2.3 and the incidence of first cousin marriages was estimated to be about 7 percent. In this population 35 families had congenital night blindness, and 33 of these families were concentrated within three large pedigrees. (8 figures, 2 tables, 17 references) Joseph E. Alfano.

Ioli-Spada, G. **A review of Russian ophthalmology for the year 1958.** Boll. d'ocul. 39:705-714, 1960.

The author reviews Russian ophthalmology for the year 1958. From this review it appears that much attention during the year was devoted to glaucoma, in particular congenital glaucoma, and glaucoma in adults associated particularly with neurologic disorders. Cyclodiathermy in the treatment of certain types of glaucoma is presented. Posterior sclerectomy seems to be much used in some types of glaucoma. A review of strabismus, (convergent, concomitant) suggests that two-thirds usually require surgery. Recessions and other operations which destroy the fascia and check ligament are condemmed. Tenotomies appear to be the vogue. A new operation for ptosis is presented, although the technique was not given in the review.

Corneal transplantations, in particular the re-innervation following transplantation, received attention, and the conclusion reached was that there is a significant increase in the innervation following surgery and this re-innervation is related in some way to clarity of the corneal graft.

A follow-up report on a case of an iris melanoma is presented. The lesion, and the ciliary body were treated by electrocoagulation and two years later the patient was well in all respects showing no evidence of either local or systemic metastases.

The surgery of stenosis of the lacrimal passage is discussed, and although the technique is not presented, the surgical approach utilizes the upper puncta and passage. In the medical treatment of glaucoma, a substance termed Diacarb which is similar to diamox is currently in vogue. A derivative of Pirazolidin is being used in the therapy of endogenous uveitis, whereas a streptomycin and nicotonic acid combination is being used in the treatment of tuberculous uveitis. A new preparation has been introduced for the treatment of corneal infections which did

not respond to the penicillin or sulfonamide preparations. A preparation called Furacilin (which seems to be related to Furacin) was condemned, and the toxicity of certain streptomycin preparations is reaffirmed.

A number of new mydriatics are being tested, among them one which produces a fall in the intraocular pressure. Of the miotics the most effective was Pleosarbin, followed in efficacy by Armin (a phosphoiodine preparation) and lastly pilocarpine. (66 references) Joseph E. Alfano.

Kamelov, M. D. and Tashkent, **The sixth scientific and practical ophthalmological meeting of Uzbekistan, held in Tashkent on April 25-26, 1960.** Vestnik Oftal. 4:87-88, July-Aug., 1961.

There are 250 ophthalmologists in Uzbekistan, 1,379 ophthalmological hospital beds and four ophthalmologic chairs. The emphasis on prevention and early diagnosis of eye disease has helped decrease the incidence of trachoma greatly since 1957-1959. Over a period of three years, 1,070 subjects were examined in a glaucoma night hospital. In a study made of 1,252 subjects only two percent were diagnosed as having clinical symptoms of glaucoma.

A great deal of research is being done for the prevention of ophthalmologic diseases. A. A. Kevayev has developed a small camera for photographing the fundus. The same apparatus can be used as an electro-ophthalmoscope for direct and indirect ophthalmoscopy.

Benjamin Ziv.

Müller, K. **Goethe's spectacles.** Klin. Monatsbl. f. Augenh. 138:882-855, 1961.

The spectacles used by Johann W. von Goethe are described and illustrated. Goethe was myopic. He had a deep-seated aversion to anyone wearing glasses, which is amusingly born out by citations from his works. Gunter K. von Noorden.

Redslob, E. **Medications which have fallen into oblivion.** Ann. d'ocul. 194:733-736, Aug., 1961.

This most amusing article by Dr. Redslob reviews some of the ancient medications used in ophthalmology. He particularly singles out those that were traditionally thought to be the last word in effectiveness. He mentions first the use of well water in rural districts, and the use of fresh milk in the city as poultices to the eye. Slightly more prosperous patients would employ a fresh piece of veal applied to the eye. This at least was cooling. Then came the era of true drugs, of which the first was probably powdered calomel. This was almost a panacea. It was quickly followed by yellow oxide of mercury, and the author states that without this it was almost impossible to practice ophthalmology. Furthermore, he feels that in certain conditions today it is still invaluable. Boric acid was widely used, and still is, and if it does no good it at least does no harm. Another panacea widely used in former days was a collyrium of zinc sulfate. Another popular collyrium was a solution of silver, either as the nitrate or as the proteinate. Unfortunately these frequently produce an argyrosis and so have fallen into disuse. Finally, he mentions subconjunctival injections, particularly of cyanide of mercury. This was used largely for luetic affections of the fundus, and apparently with good results. The author closes with a plea not to forget some of these old remedies since they are still useful in selected situations. David Shoch.

Schirmer, R. **The old Egyptian eye myths. I. The legend of the sun eye. II. The legend of the moon eye.** Klin. Monatsbl. f. Augenh. 138:887-888, 1961.

This is an excursion into Egyptian mythology where sun and moon at one time were considered to be the eyes of the god Horus. 9 references)

Gunter K. von Noorden.

NEWS ITEMS

EDITED BY DONALD J. LYLE, M.D.
411 Oak Street, Cincinnati 19, Ohio

News items should reach the editor by the 10th of the month. For adequate publicity, notice of postgraduate courses and meetings should be received three months in advance.

DEATHS

Dr. Babbitt O. Miller, Portland, Oregon, died July 14, 1961, aged 82 years.

Dr. Rose Carmel Cacchillo, New York City, died July 9, 1961, aged 40 years.

Dr. Alfred Kestenbaum, New York City, died July 17, 1961, aged 71 years.

ANNOUNCEMENTS

NEW YORK UNIVERSITY COURSES

New York University Post-Graduate Medical School, Department of Ophthalmology, offers the following courses:

Ophthalmic plastic surgery. February 26th through March 2nd: Part-time course, from 2:00 to 5:00 P.M., under the direction of Dr. Sidney A. Fox. Covers essentials of ophthalmic plastic surgery for the practicing ophthalmologist. Tuition: $90.00.

Motor anomalies of the eye. Part I: March 5th through 10th. Tuition: $115.00. Part II: March 12th through 16th. Tuition $100.00. Full-time course given in two parts, under the direction of Dr. Harold W. Brown. Case demonstrations follow the lectures. Part II is a continuation of first course.

Surgery of the eye. March 19th through 24th. Full-time course, under the direction of Dr. Rudolf Aebli. Consists of lectures on cataract surgery, glaucoma, ocular muscles and so forth. Practical work on technique on the cadaver. Maximum class: 11. Tuition: $140.00.

Ophthalmoscopy. April 23rd through 27th. Part-time course from 9:00 A.M. to 12:00 noon, under the direction of Dr. George N. Wise. Study of normal fundus, congenital anomalies, diseases of the vitreous, retina, choroid and so forth. Illustrations with Kodachrome slides and case presentations. Tuition: $60.00.

Histopathology. April 23rd through 27th. Part-time course from 1:00 to 4:00 P.M., under the direction of Dr. A. Marvin Gillman. Lectures, demonstrations and microscopic study of exemplary pathologic material covering a variety of subjects. Tuition: $100.00.

For additional information, write to Associate Dean, New York University Medical Center 550 First Avenue, New York 16, New York.

FLORIDA MIDWINTER SEMINAR OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

The 16th, Annual Florida Midwinter Seminar in Ophthalmology and Otolaryngology will convene January 29th and continue through February 3rd. The Americana at 9701 Collins Avenue, Miami Beach, has again been chosen for this year's meeting. The lectures on ophthalmology will be presented on January 29th, 30th and 31st. The lecturers for these courses will be, A. B. Reese, M.D., New York, Lorenz E. Zimmerman, M.D., Washington, D.C., Byron Smith, M.D., New York, Donald M. Shafer, M.D., New York, and Albert E. Sloane, M.D., Boston.

All the meetings will be held at the Americana Hotel. The registration fee for the seminar is $50.00. A check for $10.00 payable to the Florida Midwinter Seminar must accompany application. This is not returnable. The remainder of the registration fee will be paid at the seminar desk at the Americana Hotel on arrival, or to avoid the congestion at the registration desk send the total amount of $50.00 with application; $40.00 will be refunded if attendance is prevented. On the division of ophthamology are Shaler Richardson, M.D., Jacksonville, Charles Boyd, M.D., Jacksonville, Joseph Taylor, Jr., M.D., Tampa, Kenneth Whitmer, M.D., Miami, Edward Norton M.D., Miami.

RESEARCH STUDY CLUB

The Research Study Club of Los Angeles announces its 31st annual midwinter convention in ophthalmology and otolaryngology January 22nd through January 26th at the Statler Hilton Hotel, Los Angeles. Guest speakers for ophthalmology will be Joaquin Barraquer, M.D., Barcelona, Spain, Mr. D. P. Choyce, F.R.C.S., professor of surgery, Royal College of Surgeons, Essex, England, Harold F. Falls, M.D., Ann Arbor, Michigan, and Jerome W. Bettman, M.D., San Francisco.

In order to become eligible for attendance at the convention, applicants must be members in good standing of the American Medical Association. The fee for the entire course or any part of it is $110.00. Checks should be made payable to Norman Jesburg, treasurer, 500 South Lucas Avenue, Los Angeles 17, California.

LOS ANGELES MEETING

The Los Angeles sectional meeting of the American College of Surgeons will be held January 29th through February 1st. The program for ophthalmic surgery is: Monday, January 29th, WARREN A. WILSON, Los Angeles, *Presiding.*

9:00-10:25 a.m. Common plastic surgery procedures in ophthalmology. *Symposium,* Robert E. Bartlett, Los Angeles, *Presiding,* Lid reconstruction, Bradley Straatsma, Conjunctivoplasty, Deane C. Hartman, Enucleation vs. evisceration, Robert E.

Bartlett, Minor plastic procedures of the lids, Frank C. Winters.

10:40 a.m.-12:00 noon: Photocoagulation in treatment of retinal detachment and other lesions of the eye, *panel discussion,* Lyle Powell, San Diego, *moderators:* Philip D. Shanedling, Los Angeles, Samuel V. Abraham, Los Angeles, and S. Rodman Irvine, Beverly Hills.

2:00-5:00 p.m., How I do it clinic, John P. Lordan, Beverly Hills, *Presiding:* Total autokeratoplasty, Joaquin Barraquer, Barcelona, Spain, Techniques of cataract extraction, D. P. Choyce, Westcliff-on-Sea, Essex, England, Eye indications for neurological intervention, David O. Harrington, Surgical treatment of bullous keratitis, George P. Landegger, Eye operating room team: Assistants, training, anesthesia, instruments, sterilization and contamination, Jerome W. Bettman, Minor and office surgery of the eye and adnexa, Michel Loutfallah, and Management of the lacerated globe, Orwyn H. Ellis.

Tuesday, January 30th, S. RODMAN IRVINE, Beverly Hills, *Presiding*

9:00-10:15 a.m., Surgical indications and operations of choice in the handling of glaucoma, *Symposium,* Robert A. Norene, Los Angeles, *Presiding:* Angle-closure glaucoma, Glenn O. Dayton, Jr., Open-angle glaucoma, Robert E. Christensen, Secondary glaucoma, S. Rodman Irvine, and Revision of glaucoma operations, George K. Kambara.

10:40-12:00 noon, Cataract surgery, *symposium,* Dudley Bell, Oakland, *Presiding:* Three decades of cataract surgery at the Los Angeles County Hospital, William J. Endres, Cataract surgery in infants and children, Fredrick C. Cordes, Long-range results of cataract surgery, Julian Dow, and Prophylaxis of some accidents and complications in lens surgery, Joaquin Barraquer.

2:00-5:00 p.m., How I do it clinic, Samuel V. Abraham, Los Angeles, *Presiding:* Acrylic lens implants in cataract surgery, D. P. Choyce, Choice of strabismus operations based on the A-V syndrome, Arthur Jampolsky, Surgical management of exotropia, Alfred R. Robbins, Complications necessitating reoperation in muscle surgery, John P. Lordan, Review of new surgical procedures in tropias and phorias, J. B. V. Butler, Psychological preparation of the patient for an ophthalmic operation, George E. Morgan, General Anesthesia in ophthalmic surgery, Joseph H. Failing, and Transplantation of parotid duct to conjunctival sac, Max K. Pierce.

PLASTIC SURGERY COURSE

A three-week intensive course in ophthalmic plastic surgery will be conducted in New York, March 12th through 30th. The course will consist of lectures, sessions in doctors' offices, preliminary and follow-up cases that are operated on during the time of the course, moving picture demonstrations of various ophthalmic plastic procedures, observation and assistance at the operating table on actual surgical cases, cadaver work, lectures and demonstrations and ancillary subjects such as photography, pathology and X-ray radiation.

The fee for the course is $250.00. Anyone interested may contact the Registrar of the Institute of Ophthalmology of the Americas, New York Eye and Ear Infirmary or any of the following: Dr. Wendell Hughes, Hempstead, New York, Dr. Byron C. Smith, New York or, Dr. J. Gordon Cole, New York.

FIRST INTERNATIONAL SYMPOSIUM

The first International Symposium of the Manhattan Eye, Ear and Throat Hospital, New York, on "Plastic and reconstructive surgery of the eye, eyelids and adnexa" will be held May 21st through 25th. The program will consist of a series of lectures, discussions, televised surgical sessions, motion picture sessions and patient presentations. An internationally recognized faculty of more than 65 men from the fields of plastic surgery, ophthalmology and otolaryngology will present material. Four days will be devoted to the cornea with emphasis on its relationship to the previously presented plastic surgical material. Papers will be presented in English, French and Spanish with simultaneous translation being provided for all participants. The didactic material presented and a summary of the discussions will be published following the meeting in book form by Butterworths, and will be available to all registrants without charge.

The honorary president is Prof. Varaztad H. Kazanjian. chairman, Prof. Richard C. Troutman; program chairmen, Prof. John M. Converse, plastic surgery; Dr. Byron Smith, ophthalmology. Executive committee: Dr. Peter H. Ballen, Prof. Joaquin Barraquer, Prof. Benjamin F. Boyd, Dr. R. Townley Paton, Dr. W. Guernsey Frey, Dr. Blair O. Rogers, Sir Benjamin Rycroft, Prof. Dr. Karl Schuchardt. Advisory committee: Dr. J. Gordon Cole, Dr. Wendell L. Hughes, Mr. Thurston H. Long, Prof. Lyndon A. Peer, Dr. Clarence Straatsma. Simultaneous translation: Dr. Eduardo Orbe and staff. Publication: Mr. Jack Burgess, Butterworths.

Free papers will not be solicited. Presentation of surgical films pertinent to the subject will be invited, subject to approval of the program committee. In each of 14 didactic sessions, a 20-minute discussion period is provided for questions and discussion. Discussion papers, not to exceed three minutes, will be accepted for this period, subject to the approval of the section chairman.

Registration is limited to 500 participants. Registration fees: $100.00 (U.S.A. and Canada) and $50.00 (other countries).

Please address inquires to: Prof. Richard C. Troutman, chairman, First International Symposium of the Manhattan Eye, Ear and Throat Hospital, 210 East 64th Street, New York 21, New York, U.S.A.

Note. During the week following the International Symposium, May 27 to June 2, 1962, a course on plastic and reconstructive surgery of the face will be given under the direction of Prof. John Marquis Converse and staff at the New York

University Medical Center. Registration will be quite limited. Those desiring to attend this meeting may also address inquiries to Prof. Troutma , which will be forwarded to Prof. Converse.

New York Alumni Association

The annual spring meeting of the Alumni Association of the New York Eye and Ear Infirmary will be held April 9th through 12th. The entire meeting will be oriented toward the subject of cataracts. Symposia will be offered on preoperative work-up, surgical management and complications of cataract surgery. There will also be courses and a closed circuit television demonstration of surgical procedures. Additional information may be obtained by writing to Dr. Vincent Carter, Jr., secretary, 218 Second Avenue, New York 3, New York.

Washington Hospital Center

Lorenz E. Zimmerman, M.D., and Arthur M. Silverstein, M.D., of the Armed Forces Institute of Pathology, will be the lecturers on the January 6th, 13th, 20th and 27th sessions of the Basic Science Lectures sponsored by the Department of Ophthalmology, Washington Hospital Center, Washington, D.C. The subject of their discussions will be "Pathology and immunochemistry."

Traineeship in pediatric ophthalmology

The Department of Ophthalmology of the Children's Hospital of Washington, D.C., offers a six-month traineeship in pediatric ophthalmology to graduates of recognized residencies in ophthalmology. The training consists of in- and out-patient hospital experience exclusively with children, pediatric ophthalmic pathology at the Armed Forces Institute of Pathology, and auditing and assisting to a limited extent in private offices. Those interested should direct inquiry to Dr. Frank D. Costenbader, 1605 22nd Street, N.W., Washington 8, D.C.

Pan-Pacific Surgical Association

The Ophthalmology Section of the ninth congress of the Pan-Pacific Surgical Association will convene in Honolulu from November 5 through 13, 1963. The first Pan-Pacific Mobile Educational Lecture Seminar will take place November 13, 1963, through December 10, 1963, in New Zealand, Australia, Thailand, Philippines, Hong Kong and Japan.

All ophthalmologists are cordially invited to attend both of these meetings. The ninth congress offers an extensive ophthalmic program with leading international ophthalmologists participating. The seminar through the Pacific area offers for the first time scientific meetings presenting medical material unique to the areas in which they will be held.

For further information write to Dr. F. J. Pinkerton, director general, Pan-Pacific Surgical Association, Suite 570, Alexander Young Building, Honolulu 13, Hawaii.

Gill meeting

The Gill Memorial Eye, Ear and Throat Hospital, Roanoke, Virginia, announces, its 35th annual spring congress in ophthalmology and otolaryngology and allied specialties, April 2nd through April 6th. Among the guest speakers are J. Gordon Cole, M.D., New York, LeRoy Crandell, M.D., Winston-Salem; David D. Donaldson, M.D., Boston; Richard T. Farrior, M.D., Tampa; Miles A. Galin, M.D., New York; W. Horsley Gantt, M.D., Baltimore; R. D. Harley, M.D., Atlantic City; R. L. Hilsinger, M.D., Cincinnati; Blaine S. Nashold, M.D., Durham; George Pack, M.D., New York; Marshall M. Parks, M.D., Washington, D.C.; A. Benedict Rizzuti, M.D., Brooklyn; A. D. Ruedemann, M.D., Detroit; Herbert O. Sieker, M.D., Durham; Byron Smith, M.D., New York; James Snead, M.D., Roanoke; P. D. Trevor-Roper, M.D., London; Richard Troutman, M.D., Brooklyn; Harry J. Warthen, M.D., and Peter Pastore, M.D., Richmond, Virginia. For further information write to Superintendent, P.O. Box 1789, Roanoke, Virginia.

Michigan course

The annual ophthalmology conference at The University of Michigan Medical Center will be held April 23, 24 and 25, 1962, under the direction of Dr. F. Bruce Fralick, chairman, Department of Ophthalmology. Applications may be addressed to the Department of Postgraduate Medicine, University Hospital, Ann Arbor, Michigan.

Minnesota courses

A medical continuation course in ophthalmology will be presented at the Center for Continuation Study, University of Minnesota, May 7, 8 and 9, 1962. For further information concerning this course, write to the Director, Department of Continuation Medical Education, 1342 Mayo Memorial, University of Minnesota 14, Minnesota.

Wills conference

The 14th annual clinical conference of the Staff and Society of Ex-Residents of Wills Eye Hospital will be held on February 15, 16 and 17, 1962. Registration will begin at 9:00 A.M. on Thursday. Ward rounds will start at 9:15 A.M. The scientific program will start at 10:00 A.M. Television surgery will be held in the afternoon. The scientific meeting of the Section on Ophthalmology, College of Physicians of Philadelphia will be held on Thursday evening, February 15. This will be preceded by dinner. Dr. Charles Schepens, director of the Retina Foundation, Boston, Massachusetts, will be the guest speaker.

The scientific program will be continued through Friday and a reception for those attending the meeting will be held Friday evening at the Barclay Hotel.

On Saturday morning the Arthur J. Bedell Lecture will be delivered by Dr. Frank Walsh, professor of ophthalmology, Johns Hopkins University, Baltimore, Maryland. The scientific session will be completed by noon. The Wills Eye Hospital Ex-Residents will have a dinner meeting on Saturday evening.

Societies

Southern Association

The Section on Ophthalmology and Otolaryngology of the Southern Medical Association, at the meeting in Dallas, Texas, November 5th to 9th, elected the following officers for 1962: chairman: Dr. Samuel McPherson, Durham, North Carolina; chairman-elect, Dr. Harold Tabb, New Orleans, Louisiana; vice-chairman, ophthalmology, Dr. Kenneth Whitmer, Miami, Florida; vice-chairman, otolaryngology, Dr. James R. Chandler, Miami, Florida; secretary: Dr. Albert C. Esposito, Huntington, West Virginia; associate secretary: Dr. Neil Callahan, Portsmouth, Virginia. Elected to the Executive Committee were: Dr. Edley Jones, Jackson, Mississippi; Dr. Alston Callahan, Birmingham, Alabama; Dr. Philip Lewis, Memphis, Tennessee; Dr. Lyle Sellers, Dallas, Texas; Dr. Ben Senturi, Saint Louis, Missouri, and Dr. Jack Jervey, Greenville, South Carolina. Other members of the Executive Committee are the three immediate past presidents: Dr. Slaughter Fitz-Hugh, Charlottesville, Virginia; Dr. George Haik, New Orleans, Louisiana; and Dr. Miles Lewis, New Orleans, Louisiana. The next meeting will be held in Miami Beach, Florida, November 12 to 17, 1962. For further information please contact the secretary, Dr. Albert C. Esposito, Huntington, West Virginia.

Miscellaneous

Denver meeting

Speakers on the ophthalmology program of the Denver Clinical meeting presented by the Council on Scientific Assembly of the American Medical Association, November 27th through 30th in Denver were John C. Long, M.D., Denver, Bayard H. Colyear, Jr., M.D., San Francisco, W. Howard Morrison, M.D., Omaha, Duane D. Lahey, M.D., Denver, Morris Kaplan, M.D., Denver, George A. Filmer, M.D., Denver, and Phillip P. Ellis, M.D., Denver. Exhibits of ophthalmic interest were shown by Raymond Hofstra, M.D. Washington, D.C., on "Prevent blindness" and by Ira A. Abrahamson, Sr., M.D., and Ira A. Abrahamson, Jr., M.D., on "Know your eyes."

Emory postgraduate course

Algernon B. Reese, M.D., New York, Charles L. Schepens, M.D., Boston, and Lorenz E. Zimmerman, M.D., Washington, D.C., were guest speakers on the postgraduate course sponsored by the Department of Ophthalmology, Emory University School of Medicine, at Grady Memorial Hospital, November 30th and December 1st.

Kansas City program

The Kansas City Society of Ophthalmology and Otolaryngology sponsored a single three-day refresher course, December 6th through 8th, in place of the regular one-day meetings for the 1961-1962 season. Speakers in ophthalmology were Peter C. Kronfeld, M.D., Chicago, David Donaldson, M.D., Boston, Max S. Lake, M.D., Salina Kansas, and Otto H. Elser, M.D., and Calvin J. Curtis, M.D., Kansas City, Kansas.

Mid-Winter research meeting

The Association for Research in Ophthalmology, Inc., held its annual midwinter meeting in Detroit, Michigan, December 4th, 5th and 6th, with V. Everett Kinsey, Ph.D., presiding. Dr. Albert M. Potts, Chicago, presented the Friedenwald Memorial Lecture.

Eye-Banks Association

The Committee on Eye-Banks of the American Academy of Ophthalmology and Otolaryngology assisted in organizing the Eye-Banks Association of America in Chicago on October 7, 1961. The chairman of the Eye-Bank Committee is R. Townley Paton, M.D., of New York. Other members are: A. D. Ruedemann, Sr., M.D., Detroit, Alfred E. Maumenee, M.D., Baltimore, Michael J. Hogan, M.D., San Francisco, A. E. Braley, M.D., Iowa City, Ramon Castroviejo, M.D., New York, and John Harry King, Jr., M.D., Washington, D.C. The two liaison members between the Eye-Banks Association of America and the American Academy of Ophthalmology are A. E. Braley, M.D., and John Harry King, Jr., M.D.

The elected Regional Board of Directors to correspond later to the Federal Communications Districts, consists of five lay Eye-Bank officers and five medical doctors. They are: F. J. Pinkerton, M.D., medical director, Hawaii Eye-Bank, Honolulu, W. B. Clark, M.D., New Orleans, Harry McCloskey, Philadelphia, Morris Kaplan, M.D., Denver, L. B. Holt, M.D., medical director, North Carolina Eye-Bank, Winston-Salem, Rudolph Spitzer, executive secretary, Buffalo Eye-Bank, Robert E. Simpson, president Southern Eye-Bank, New Orleans, Mrs. Mayda Roberts, executive secretary, Washington, D.C. Eye-Bank, Rosario J. Guglielmino, president Rochester (New York) Eye-Bank, Ted Hunter, president Iowa Eye-Bank. Each Eye-Bank that is a member of the Eye-Banks Association of America has one delegate or an alternate to elect the Board of Directors at an annual meeting.

The purposes are: (1) form an association of member Eye-Banks for the purpose of establishing uniform standards and procedures; (2) exchange of information from member Eye-Banks; (3) establishment of central and regional clearing houses; (4) to promote establishment of new Eye-Banks where needed; (5) promotion of eye research; (6) to promote co-operation between lay and professional groups operating in eye-bank field; (7) to be a center of information in all matters pertaining to eye-bank organization and operation.

The officers elected are: Treasurer, Rudolph Spitzer, Buffalo Eye-Bank & Research Society, Inc., 2550 Main Street Buffalo 14, New York; secretary, Mrs. Mayda Roberts, Eye-Bank & Research Foundation, 333 Carroll Street, N.W., Washington, D.C.; vice presidents, F. J. Pinkerton, M.D., The Eye-Bank, Queens Hospital Grounds, Honolulu 13, Hawaii; Robert L. Simpson, M.D., president Southern Eye-Bank, New Orleans, Louisiana;

Morris Kaplan, M.D., Denver, Colorado. President, Mr. Rosario J. Guglielmino, 16 State Street, Rochester 14, New York, is a practicing attorney and president of the Rochester Eye-Bank and Research Society. The president-elect is Dr. L. B. Holt, medical director of the North Carolina Eye-Bank.

National Medical Foundation

Marking the fifth anniversary of its founding in Chicago, in October, 1956, the National Medical Foundation For Eye Care re-elected Ralph O. Rychener, M.D., of Memphis, president; William B. Clark, M.D., New Orleans, vice president, succeeding Barnet R. Sakler, M.D., of Cincinnati, Ohio, who became chairman of the executive committee, Charles E. Jaeckle, M.D., of Defiance, Ohio, was re-elected secretary and treasurer. Named to the executive committee along with Dr. Rychener, ex officio, Dr. Sakler, chairman, Dr. Clark and Dr. Jaeckle, were Laurence R. Dame, M.D., of Greenfield, Massachusetts, and Howard F. Hill, M.D., of Waterville, Maine.

Three new members were elected to the Board of Trustees for terms of three years each: Dr. Robert J. Beitel, Jr., M.D., of Allentown, Pennsylvania, Bernard Kronenberg, M.D., New York, and Thomas J. Vanzant, M.D., Houston, Texas. They will serve with the following members of the Board whose terms continue until 1962 and 1963; Alson E. Braley, M.D., Iowa City, Purman Dorman, M.D., Seattle, J. Spencer Dryden, M.D., Washington, D.C., John L. Matthews, M.D., San Antonio, S. D. McPherson, Jr., M.D., Durham, A. D. Ruedemann M.D., Detroit, Derrick Vail, M.D., Chicago, and Warren A. Wilson, M.D., Los Angeles.

Harold F. Falls M.D., Ann Arbor, who served last year as chairman of the executive committee, and Harold G. Scheie, M.D., Philadelphia, a member of the executive committee last year, were both named to the Foundation's Board of Advisors, in which capacity they will serve with William L. Benedict, M.D., Rochester, Minnesota, Frederick C. Cordes, M.D., San Francisco, Everett L. Goar, M.D., Houston, Donald J. Lyle, M.D., Cincinnati, Algernon B. Reese, M.D., New York.

Elected chairman of the Foundation's Board of Councilors for 1961-62 was Norbert F. Alberstadt, M.D., Erie, Pennsylvania, Charles A. Young, M.D., Roanoke, Virginia, was named vice chairman, and Robert L. Tour, M.D., San Francisco, secretary.

The Foundation, an agency devoted to public education concerning the elements of good medical eye care, announced that its first annual Helmholtz Memorial Award for outstanding nonmedical writing in the field of eye care, had been won by John Kord Lagemann of New York, for his article in the May, 1960, issue of *Redbook Magazine* entitled "The facts about your eyes." The award carries a cash prize of $250.00. Approximately 4,000,000 pieces of literature covering various aspects of eye care, including five public-information leaflets and seven reports, have been distributed by the Foundation.

Personals

Dr. G. E. Jayle, Professor of ophthalmology, Faculty of Medicine, Marseille, France, was guest speaker at a meeting of the Montreal Ophthalmological Society, held at Hotel Dieu Hospital, Montreal, September 26, 1961, Dr. Jayle spoke on "Examination of the visual field in mesopic illumination."

Dr. Alston Callahan, Birmingham, Alabama, addressed the general assembly of the Kentucky State Medical Association at its annual meeting in Louisville. Dr. Callahan participated in a panel on trauma, the members of which were Dr. Garrett Pipkin of Kansas City, Missouri, Dr. Virgil A. Plessinger and Dr. Jerome F. Wiot of Cincinnati, Ohio, and the moderator, Dr. Charles G. Child of Ann Arbor, Michigan. An original paper was presented before the assembly on "Sight saving measures for the general practitioner." At the sectional meeting, Dr. Callahan spoke on "Newer concepts of ophthalmic plastic surgery," and at the annual dinner meeting, "Newer concepts of surgery of the globe."

The Journal announces with regret the death on September 10th at Saint Louis, Missouri, of Mr. Charles R. Storz, chairman of the board of the Storz Instrument Company.

URGENT REQUEST

The Uveitis Laboratory, University of California School of Medicine, San Francisco, is vitally interested in obtaining freshly enucleated eyes from patients with all types of uveitis and other endogenous inflammations. Attempts are being made to isolate etiologic agents from these eyes.

The eyes should be placed in a sterile bottle, packaged with the history and findings, and shipped as quickly as possible. Please send specimens special delivery, collect, and mark the package "Fresh Tissue Specimen—Rush." Do not freeze or use preservatives of any kind.

A report of isolations of organisms and pathologic findings, including a slide, will be sent to the contributor. Credit will be given in any resulting publications if desired.

Telegraph collect if specimen being sent.

Send eyes to

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New BLEPHAMIDE Ophthalmic Liquifilm is a basic advance in the management of blepharitis. The potent and proven antiseborrheic/antistaphylococcal formula treats the underlying disorder while the rapid-acting anti-inflammatory/decongestant relieves pain and inflammation and improves the eye's appearance. Convenient, well tolerated virtually non-stinging, BLEPHAMIDE provides truly effective, one-prescription 24-hour therapy.

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